PB88-180450

Health and Environmental Effects Profile for Nitrophenols

(U.S.) Environmental Protection Agency
Cincinnati, OH

Sep 85

U.S. Department of Commerce
National Technical Information Service
NTIS

PB88-180450

EPA/600/X-85/354
September 1985

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR NITROPHENOLS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA/600/X-85/354	2.	3. RECIPIENT'S ACCESSION NO. PB88 180450/AS
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Nitrophenols		5. REPORT DATE September 1985 6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS		10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268		13. TYPE OF REPORT AND PERIOD COVERED 14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES		

16. ABSTRACT

The Health and Environmental Effects Profile for nitrophenols was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for nitrophenols.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a relase as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Public	Unclassified	98
	20. SECURITY CLASS (This page) Unclassified	22. PRICE PC 14.95 / MF 4.95

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1984.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	1
1.3.	PRODUCTION DATA	1
1.4.	USE DATA	6
2.	ENVIRONMENTAL FATE AND TRANSPORT PROCESSES	10
2.1.	WATER	10
2.1.1.	Hydrolysis	10
2.1.2.	Oxidation	10
2.1.3.	Photolysis	11
2.1.4.	Microbial Degradation	12
2.1.5.	Transport	16
2.2.	AIR	18
2.3.	SOIL	19
2.3.1.	Microbial Degradation	19
2.3.2.	Chemical Degradation	20
2.3.3.	Photolysis	20
2.3.4.	Leaching -- Adsorption	21
2.3.5.	Volatilization	22
2.3.6.	Persistence	23
2.4.	SUMMARY	23
3.	EXPOSURE	24
3.1.	WATER	24
3.2.	FOOD	25
3.3.	INHALATION	25
3.4.	DERMAL	25
4.	PHARMACOKINETICS	28
4.1.	ABSORPTION	28
4.2.	DISTRIBUTION	28
4.3.	METABOLISM	29
4.4.	EXCRETION	30

TABLE OF CONTENTS (cont.)

		Page
5.	EFFECTS	34
5.1.	CARCINOGENICITY	34
5.2.	MUTAGENICITY	34
5.3.	TERATOGENICITY	42
5.4.	OTHER REPRODUCTIVE EFFECTS	42
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	42
5.6.	OTHER RELEVANT INFORMATION	42
6.	AQUATIC TOXICITY	48
6.1.	ACUTE TOXICITY	48
6.2.	CHRONIC AND SUBCHRONIC TOXICITY	50
6.3.	PLANT EFFECTS	51
6.4.	RESIDUE	52
6.5.	OTHER RELEVANT INFORMATION	52
7.	EXISTING GUIDELINES AND STANDARDS	54
7.1.	HUMAN	54
7.2.	AQUATIC	54
8.	RISK ASSESSMENT	55
9.	REPORTABLE QUANTITIES	57
9.1.	REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY	57
9.2.	WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY	57
10.	REFERENCES	59
APPENDIX:	LITERATURE SEARCHED	87

LIST OF TABLES

No.	Title	Page
1-1	Structures, CAS Numbers, Molecular Weights and Empirical Formulas of the Nitrophenols	2
1-2	Physical Properties of 2-Nitrophenol	3
1-3	Physical Properties of 3-Nitrophenol	4
1-4	Physical Properties of 4-Nitrophenol	5
1-5	1977 Production Data for Nitrophenols	7
3-1	U.S. EPA STORET Data for 2-Nitrophenol	26
3-2	U.S. EPA STORET Data for 4-Nitrophenol	27
4-1	Cumulative percentages of the Dose Excreted in Urine and Bile as p-Nitrophenol, and as its Glucoronide and Sulfate, in the 24 Hours Following Femoral Vein Administration of 4-Nitrophenol to Rats	32
5-1	Animal. Agent: 2-Nitrophenol	35
5-2	Animal. Agent: 4-Nitrophenol	36
5-3	Mutagenicity of 2-Nitrophenol	37
5-4	Mutagenicity of 3-Nitrophenol	38
5-5	Mutagenicity of 4-Nitrophenol	40
5-6	Acute Toxicity of Orally Administered Mononitrophenols	43
9-1	Minimum Effective Dose (MED) and Reportable Quantity (RQ)	58

LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
ATP	Adenosine triphosphate
BCF	Bioconcentration factor
BODT	Biochemical oxygen demand, theoretical
bw	Body weight
CAS	Chemical Abstracts Service
COD	Chemical oxygen demand
DNA	Deoxyribonucleic acid
DOC	Dichromate oxygen consumed
EC_{50}	Median effective concentration
HPLC	High performance liquid chromatography
K_b	Mean microbial transformation rate constant
K_{oc}	Soil sorption coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dosage levels)
LC_0	No-effect concentration
LD_{50}	Dose lethal to 50% of recipients (and all other subscripted dosage levels)
MATC	Maximum acceptable toxicant concentrations
NADH	Nicotinamide adenine dinucleotide (reduced form)
ppb	Parts per billion
ppm	Parts per million
SD	Standard deviation
UV	Ultraviolet
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The structures, CAS Registry numbers, molecular weights and empirical formulas of the nitrophenols are presented in Table 1-1. The CAS number for an isomeric mixture of the nitrophenols is 25154-55-6.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Physical properties of each of the nitrophenols are listed in Tables 1-2, 1-3 and 1-4.

Chemically, the nitro group on the benzene ring enhances the acidity of the hydroxyl group, making the nitrophenols much stronger acids than phenol. 2-Nitrophenol is volatile in steam and is relatively soluble in nonassociated solvents such as benzene, whereas 3-nitrophenol and 4-nitrophenol are not steam volatile and are more soluble in polar solvents. The three mononitrophenols are reduced easily to the corresponding aminophenols (Matsuguma, 1967).

1.3. PRODUCTION DATA

2-Nitrophenol is manufactured commercially in the United States by Monsanto in Sauget, IL (SRI, 1984; USITC, 1984a), and has been produced in amounts of ~10-15 million pounds/year (Howard et al., 1976). 4-Nitrophenol is manufactured by Monsanto in Anniston, AL and by DuPont in Deepwater, NJ (SRI, 1984; USITC, 1984a), at volumes of 36 and 10 million pounds/year, respectively (CMR, 1984). The Monsanto production of 4-nitrophenol is captively consumed (SRI, 1984). The industrial demand for 4-nitrophenol in 1983 and 1984 was estimated to be 25 and 33 million pounds, respectively (CMR, 1984), which is indicative of production volume. Although SRI (1984) and USITC (1984a) do not list 3-nitrophenol as a commercially manufactured chemical, it is probably produced in limited quantities as a laboratory reagent.

TABLE 1-1

Structures, CAS Numbers, Molecular Weights and Empirical Formulas of the Nitrophenols

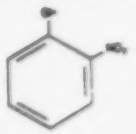
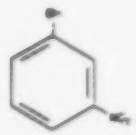
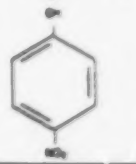
Synonym	CAS Number	Molecular Weight	Empirical Formula	Structure
2-Nitrophenol o-nitrophenol 2-hydroxynitro-benzene	88-75-5	139.11	$C_6H_5NO_3$	
3-Nitrophenol m-nitrophenol 3-hydroxynitro-benzene	554-84-7	139.11	$C_6H_5NO_3$	
4-Nitrophenol p-nitrophenol 4-hydroxynitro-benzene	100-02-7	139.11	$C_6H_5NO_3$	

TABLE 1-2

Physical Properties of 2-Nitrophenol

Property	Value	Reference
Description	pale yellow crystals	Hawley, 1977
Melting point	45°C	Verschueren, 1983
Boiling point	214-217°C	Verschueren, 1983
Specific gravity	1.295 (45°C)	Hawley, 1977
pKa	7.230	Serjeant and Dempsey, 1979
Vapor pressure (mm Hg):		
at 49.3°C	1	Perry and Chilton, 1973
at 76.8°C	5	Perry and Chilton, 1973
at 20°C	0.23	Weber et al., 1981
at 20°C	0.152	Mabey et al., 1981
at 25°C	0.11	Scala and Banerjee, 1982
Water solubility:		
at 20°C	2100 ppm	Verschueren, 1983
at 100°C	10,800 ppm	
Log K_{ow}	1.79	Hansch and Leo, 1981
Henry's Law Constant (at 20°C)	7.56×10^{-6} atm-$m^3 mol^{-1}$	Mabey et al., 1981
Non-aqueous solubility	soluble in alcohol, ether	Perry and Chilton, 1973

TABLE 1-3

Physical Properties of 3-Nitrophenol

Property	Value	Reference
Description	colorless to yellow crystals	Verschueren, 1983
Melting point	96°C	Verschueren, 1983
Boiling point	194°C (70 mm Hg)	Verschueren, 1983
Specific gravity	1.485 (20/4°C)	Hawley, 1977
pKa	8.360	Serjeant and Dempsey, 1979
Vapor pressure (mm Hg): at 20°C	0.75	Weber et al., 1981
Water solubility:		
at 20°C	1.35/100 parts	Perry and Chilton, 1973
at 25°C	13,500 ppm	Verschueren, 1983
Log K_{ow}	2.00	Hansch and Leo, 1981
Non-aqueous solubility	soluble in alcohol, ether	Perry and Chilton, 1973

TABLE 1-4

Physical Properties of 4-Nitrophenol

Property	Value	Reference
Description	yellowish crystals	Hawley, 1977
Melting point	114°C	Verschueren, 1983
Boiling point	279°C (decomposes)	Verschueren, 1983
Specific gravity	1.479 (20°C)	Verschueren, 1983
pKa	7.156	Serjeant and Dempsey, 1979
Vapor pressure (mm Hg:)		
at 20°C	0.75	Weber et al., 1981
at 146°C	2.2	Mabey et al., 1981
Water solubility: at 25°C	16,000 ppm	Verschueren, 1983
Log K_{ow}	1.91	Hansch and Leo, 1981
	1.85	Geyer et al., 1984
Henry's Law Constant (at 25°C)	2.5×10^{-5} atm-$m^3 mol^{-1}$	Mabey et al., 1981
Non-aqueous solubility	soluble in alcohol, ether	Perry and Chilton, 1973

Available production data for 1977 are listed in Table 1-5 (U.S. EPA, 1977). Imports of 2- and 4-nitrophenol through principal United States customs districts in 1983 were 3.56 and 0.61 million pounds, respectively (USITC, 1984b).

2-Nitrophenol is produced by the catalytic hydrolysis of 2-nitrochlorobenzene with NaOH, while 4-nitrophenol is manufactured by the catalytic hydrolysis of 4-nitrochlorobenzene with NaOH. 3-Nitrophenol can be prepared by the diazotization of 3-nitroaniline followed by hydrolysis (Matsuguma, 1967).

1.4. USE DATA

2-Nitrophenol is used mainly in the synthesis of 2-aminophenol, 2-nitroanisole and other dyestuffs (Matsuguma, 1967). Apparently, 2-aminophenol is the major single derivative; it is a principal intermediate in a variety of industrial dye syntheses and is used as a commercial developer in photography (Farris, 1978). 2-Nitrophenol is also used in the synthesis of other chemicals and as an analytical indicator.

3-Nitrophenol has been used in the synthesis of 3-aminophenol, but this use has declined (Matsuguma, 1967), and 3-aminophenol usually is manufactured commercially by other processes. 3-Nitrophenol is used as an analytical indicator (Hawley, 1977), and can also be used as an intermediate in organic synthesis.

The percentages of the total amount of 4-nitrophenol produced and the applications are as follows (CMR, 1984):

Uses	% of Total Production
Ethyl and methyl parathions	84
n-Acetyl-4-aminophenol (APAP)	8
Other	8

TABLE 1-5

1977 Production Data for Nitrophenols*

Producer and Location	Type of Production	Production Range (lbs)
2-Nitrophenol		
Monsanto Co. Sauget, IL	manufacturer	10-50 million
Alpine Laboratories Bay Minette, AL	manufacturer	<1000
DuPont de Nemours and Co. Deepwater, NJ	manufacturer	confidential
FMC Corp. Baltimore, MD	importer	1-10 million
American Hoechst Bridgewater, NJ	importer	confidential
3-Nitrophenol:		
Eastman Kodak Rochester, NY	manufacturer	<1000
Carroll Products Wood River Junction, RI	production limited to on-site use	none
4-Nitrophenol:		
Monsanto Co. Anniston, AL	manufacturer	10-50 million
Alpine Laboratories Bay Minette, AL	manufacturer	<1000
Process Division of UOP Inc. Shreveport, LA	manufacturer	confidential
E.I. DuPont de Nemours Deepwater, NJ	manufacturer	confidential

TABLE 1-5 (cont.)

Producer and Location	Type of Production	Production Range (lbs)
4-Nitrophenol (cont.):		
American Hoechst Bridgewater, NJ	importer	confidential
Rhone-Poulenc Freeport, TX	importer	none
Conray Chemicals Rockville Centre, NY	importer	none

*Source: U.S. EPA, 1977

Other uses include intermediate applications in dye production, fungicides, photochemicals, pharmaceuticals and leather preservatives (CMR, 1984; Matsuguma, 1967).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

The fate of nitrophenols in the environment will depend upon the ability of the compounds to undergo chemical, photochemical and biological reactions and to transport or partition from one environmental matrix into another.

2.1. WATER

2.1.1. Hydrolysis. 2-Nitrophenol and 4-nitrophenol do not undergo environmental hydrolysis in either neutral, acidic or basic waters (Mabey et al., 1981). It is unlikely, therefore, that 3-nitrophenol will undergo any significant environmental hydrolysis.

2.1.2. Oxidation. Chemical oxidation of organic chemicals in aquatic environments may occur due to several different oxidants, such as singlet oxygen ($^1O_2$), alkyl peroxyl radical ($RO_2\cdot$) and hydroxyl radical ($\cdot OH$), which are generated primarily in water by sunlight-induced photochemical reactions (Mabey et al., 1981). These investigators determined that, for both 2- and 4-nitrophenol, the oxidation rate constants at 25°C for reaction with $^1O_2$ and $RO_2\cdot$ are $<2\times10^5$ and 2×10^6 M^{-1} $hour^{-1}$, respectively. Laboratory studies have shown that $RO_2\cdot$ radical concentrations of $\sim1\times10^{-9}$ M may be present in the surface waters of sunlit water bodies (Mabey et al., 1981). Assuming that there are 10 hours of sunlight/day, a half-life of ~34 days can be calculated with respect to $RO_2\cdot$ radicals. Reaction with $^1O_2$ will be considerably slower, as $\sim1\times10^{-12}$ concentrations of $^1O_2$ may be formed in sunlit natural waters (Mabey et al., 1981).

Suarez et al. (1970) and Gunther et al. (1971) demonstrated that hydroxyl radicals attack 2- and 4-nitrophenol at the C-2 and C-4 positions, resulting in the formation of complex mixtures of which hydroquinone and

1,4-benzoquinone are products. No information was found, however, from which an environmentally relevant rate could be estimated for this reaction. Kotzias et al. (1982) reported that 4-nitrophenol reacts quite rapidly with hydroxyl radicals in water in the presence of nitrate or nitrite; sunlight reacts with nitrite or nitrate and water to produce an elevated concentration of •OH.

2.1.3. Photolysis. The UV spectra for 2- and 4-nitrophenol in aqueous solution show considerable absorption in the environmentally significant range of >290 nm (Schultz, 1983; Mabey et al., 1981). 3-Nitrophenol also exhibits considerable absorption at >290 nm in aqueous solution (Weast, 1972). This absorption rate indicates a significant potential for direct photolysis.

Lemaire et al. (1982) calculated aqueous environmental photolysis rates for 4-nitrophenol at near-surface conditions by experimentally measuring the quantum yield of disappearance at different pHs and using noontime, summer conditions in Chicago as an environmental parameter. At pH 1.4, pH 5.5 (in distilled water) and pH 11.5, the calculated half-lives are 26.0, 27.5 and 32.3 hours, respectively.

Hustert et al. (1981) used the U.S. EPA test for photodegradation of chemicals in water exposed to sunlight to determine 4-nitrophenol photolysis half-lives of 5.7 days at pH 5; 6.7 days at pH 7; and 13.7 days at pH 9. Kotzias et al. (1982) exposed an aqueous solution of 4-nitrophenol to UV irradiation at >290 nm and observed a half-life of 16 hours. Nakagawa and Crosby (1974) identified 4-nitrocatechol, hydroquinone and a nonvolatile polymer as photolysis products of 4-nitrophenol.

Although aqueous photolysis rates for 2- and 3-nitrophenol are not available, the data available for 4-nitrophenol suggest that direct photolysis of the 2- and 3-isomers is likely to be environmentally significant.

Data pertaining to the sensitized photolysis of the nitrophenols were not located in the available literature as cited in the Appendix.

2.1.4. Microbial Degradation. Gerike et al. (1984) tested the biodegradability of 3-nitrophenol with a modified Coupled Units Test and found that the compound is completely degraded without yielding a recalcitrant metabolite. Kool (1984) examined the influence of different types and amounts of inocula on the biodegradation of 4-nitrophenol using the Modified OECD test. Rhine River sediment could not degrade 4-nitrophenol in 28 days, while garden soil inoculum gave about 80% degradation in 28 days. Effluent from an activated sludge plant degraded 90% 4-nitrophenol in 14 days at a 19 mg/ℓ concentration, but showed no degradation at 94 mg/ℓ. These data indicate that the biodegradability of nitrophenols depends on the kinds of inocula present and the concentration of the substrate. Using sludge from a primary digester, Shelton and Tiedje (1984) determined that 2- and 4-nitrophenol are susceptible to anaerobic biodegradation to CH_4 + CO_2. Johnson and Young (1983) found that the ability of 2- and 4-nitrophenol to be anaerobically digested decreases as the concentration of the nitrophenol increases from 1-100 mg/ℓ.

Spain and Van Veld (1983) and Van Veld and Spain (1983) measured the degradation of 4-nitrophenol in samples from freshwater, marine and estuarine sites. The half-life from the biodegradation of 4-nitrophenol in Escambria River, FL was >5 days. When the water was previously exposed to 4-nitrophenol, however, the biodegradation half-life was reduced to <40 hours, presumably due to adaptation by the microorganisms. Samples from estuarine and marine sites did not show any increase in the rate of degradation as a result of previous exposure. The biodegradation half-life for 4-nitrophenol in marine and estuarine ecocore (water plus sediment) was

>12.5 days. Rubin and Alexander (1983) found that 4-nitrophenol undergoes mineralization in water inoculated with cells from natural lakes and streams in which a natural nutrient is present. Paris et al. (1983) measured the K_b of 4-nitrophenol in five pond and river waters to be 3.8×10^{-11} ℓ/organism-hour; Paris et al. (1982) measured the K_b for 4-nitrophenol in water cultured with Pseudomonas putida U to be 1×10^{-13} ℓ/organism-hour, with 4-nitrocatechol as a metabolite.

Subba-Rao et al. (1982) measured the mineralization rate constant for 4-nitrophenol in natural lake water at concentrations of 0.60-14 pg/ℓ to 198 ng/ℓ to be 0.018-0.051 day^{-1} (half-life of 14-38 days). Rott et al. (1982) tested the biodegradability of 4-nitrophenol and found the following results: 1) GSF Test (5-day), 35% degradation, 1% degradation to CO_2; 2) Zahn-Wellens Test, 8% degradation in 14 days; 3) Modified OECD Test, 1% degradation; 4) Closed Bottle Test, 55% BODT in 28 days. Gvozdyak et al. (1982) found that 10 Bacillus species and Pseudomonas aeruginosa isolated from activated sludge were capable of rapidly degrading 4-nitrophenol. DeWalle et al. (1982) found insignificant anaerobic digestion of 2-nitrophenol in a municipal sewage treatment plant.

Liu (1981) determined a biodegradation half-life of 4-nitrophenol in water to be 2.1 days under aerobic conditions and 2.8 days under anaerobic conditions in the presence of organic nutrients; however, in the absence of organic nutrients, a half-life of 590 days was calculated. Using a static-culture flask-screening procedure, Tabak et al. (1981) examined the biodegradability of 114 organic priority pollutants to determine the extent of microbial degradation and to determine the acclimation periods; 2- and 4-nitrophenol were found to be significantly biodegradable with rapid adaptation. Means and Anderson (1981) tested the biodegradability of

4-nitrophenol and found the following results: 1) BOD test, slow degradation; 2) Shake-Flask test, 50% DOC removal in 21 days; 3) CO_2 Evolution test, 100% CO_2 evolution; 4) Gledhill test, rapid degradation; 5) Activated sludge test, slow degradation. Mabey et al. (1981) estimated the K_b values for 2- and 4-nitrophenol in water to be $3x10^{-9}$ and $1x10^{-7}$ mℓ/cell-hour, respectively.

Spain et al. (1980) found that river water that was previously exposed to 4-nitrophenol degraded the nitrophenol at a significantly faster rate than did control river water; numbers of nitrophenol-degrading bacteria increased 4-5 orders of magnitude during adaptation. Zahn and Wellens (1980) measured an 88% degradation of 3-nitrophenol in 10 days in adapted sludge and 15 days in unadapted sludge. Kawasaki (1980) and Sasaki (1978) reported that the Japanese MITI test supports the conclusions that 4-nitrophenol resists degradation. Using a CO_2 evolution test, Gilbert and Lee (1980) found 4-nitrophenol to yield 90% of theoretical CO_2 evolution in 25 days.

Gerike and Fischer (1979) tested the biodegradability of 2-nitrophenol and found the following results: 1) Coupled Units, 61% DOC removal in 7 days; 2) Zahn-Wellens test, 80% DOC removal in 14 days; 3) MITI test, 0% g BODT in 14 days; 4) AFNOR test, 16% DOC removal; 5) Sturm test, 32% of CO_2 evolution, 43% DOC removal; 6) OECD screening test, 100% DOC removal; 7) Closed-Bottle test, 0% BODT in 30 days.

Spain et al. (1979) found that a Moraxella sp. isolated from activated sludge was capable of oxidizing 4-nitrophenol to form hydroquinone and nitrite. Barth and Bunch (1979) using a static mineral salts medium with settled wastewater inocula, determined that 81.0-98.5% of the initially present 2-nitrophenol was degraded during the initial and three subculture

weekly test periods. Dojlido (1979) found 4-nitrophenol to be readily degraded by activated sludge, while Kitano (1978) found 2- and 4-nitrophenol resistant to degradation by an activated sludge in Japan. Haller (1978) found the lag period for the degradation of 16 ppm of all three nitrophenols by a wastewater to be 3-5 days. McCormick et al. (1976) found that enzyme preparations of Veillonella alkalescens are capable of reacting with all three nitrophenols. Using an actived sludge (acclimated) and mineral salts medium, Pitter (1976) measured the biodegradation rates of 2-, 3- and 4-nitrophenol and found them to be 14.0, 17.5 and 17.5 mg COD/g-hour respectively, with 95-97% removal based on COD.

Chambers et al. (1963) examined the degradation of aromatic compounds by phenol-adapted bacteria; 2-, 3- and 4-nitrophenol were found to have BODTs of 22% (3.5 hours), 30% (3.5 hours) and 22% (3 hours), respectively. Kramer and Doetsch (1950) observed that the three nitrophenols were not degraded by phenol-degrading bacteria after 5 days at 30°C.

The biodegradation data cited above, though extensive, are somewhat contradictory. It appears, however, that the ability of the nitrophenols to undergo biodegradation depends on the kinds of inocula present. Also, the concentration of the nitrophenols can be a determining factor, as certain levels may be toxic to the microorganisms present. Various biodegradation tests, as cited above, suggest that the nitrophenols are degradable, while other tests suggest that they are degradation resistant. Tests using natural waters (Spain and Van Veld, 1983; Rubin and Alexander, 1983; Paris et al., 1983; Subba-Rao et al., 1982; Liu, 1981; Spain et al., 1980) have shown, however, that the nitrophenols are capable of being biodegraded significantly in various natural ambient surface waters.

2.1.5. Transport. The transport of the nitrophenols in the aquatic environment will depend on the ability of compounds to volatilize, to adsorb to particulate organic matter and sediment, and to bioaccumulate in aquatic organisms.

2.1.5.1. VOLATILIZATION -- Pertinent data regarding the volatilization rates of the nitrophenols from water were not located in the available literature as cited in the Appendix. Mabey et al. (1981) calculated the Henry's Law Constant for 2-nitrophenol (20°C) and 4-nitrophenol (25°C) to be 7.56×10^{-6} and 2.5×10^{-5} atm-m³/mol, respectively. These values suggest that volatilization may not be significant (Lyman et al., 1982). The pKa values of 7.23 and 7.156 (see Section 1.2.) indicate that a significant fraction of these nitrophenols will be dissociated in water. This may further limit the aqueous volatilization rates, indicating that volatilization is not likely to be environmentally significant relative to photolysis, oxidation and microbial degradation.

2.1.5.2. ADSORPTION -- Pertinent data regarding the adsorption of the nitrophenols in the aquatic environment were not located in the available literatureas cited in the Appendix. U.S. EPA (1980b) developed an adsorption isotherm for nitrophenols using pulverized activated carbon. They fitted the data to the logarithmic form of the Freundlich equation:

$$\log X/M = \log K + 1/n \log C_f.$$

where:

X = $C_o - C_f$ is the amount of compound adsorbed from a given volume of solution

M = the weight of activated carbon

C_o = the amount of compound in the untreated solution

C_f = the amount of compound remaining in the treated water.

For nitrophenols of at pH of 3.0, 5.5 and 9.0 they determined the coefficient of K and 1/n to be 101, 99, 85 and 0.26, 0.34, 0.39, respectively, for 2-nitrophenol and 80.2, 76.2, 71.2 and 0.17, 0.25, 0.28, respectively, for 4-nitrophenol. The relevance of activated carbon adsorption to soil adsorption coefficient is uncertain. Soil adsorption data presented in Section 2.3.4. suggest that the nitrophenols can be moderately sorbed to sediment. In view of the paucity of available data, the relative importance of adsorption in the aquatic environment cannot be determined.

2.1.5.3. **BIOACCUMULATION** -- Geyer et al. (1981) experimentally determined the bioaccumulation factor for 4-nitrophenol with the green alga, Chlorella fusca, to be 11. In a later publication, however, Geyer et al. (1984) reported an experimental bioaccumulation factor in C. fusca to be 30.

Call et al. (1980) exposed fathead minnows to sublethal concentrations of ^{14}C-4-nitrophenol in a glass-chamber study for a 28-day period and observed a whole-body ^{14}C-bioconcentration factor of 180; the depuration half-life in this system was observed to be 228 hours. 4-Aminophenol was identified as a metabolite.

Veith et al. (1979) experimentally measured a BCF of 126 for 4-nitrophenol in fathead minnows, in an aquarium study. Freitag et al. (1982) observed a 3-day BCF of 57 for 4-nitrophenol in a static fish test study.

The BCF values for organic compounds can be predicted from the WS by Equation 2-1, developed by Kenaga and Goring (1978):

$$\log BCF = 2.79 - 0.564 \log WS \text{ (in ppm)} \qquad (2\text{-}1)$$

For 2-, 3- and 4-nitrophenol, the BCF values are calculated to be 8.0, 3.0 and 0.5, respectively. The BCF value can be predicted from the K_{ow} from Equation 2-2, developed by Veith et al. (1980):

$$\log BCF = 0.76 \log K_{ow} - 0.23 \qquad (2\text{-}2)$$

For 2-, 3- and 4-nitrophenol, the BCF values are calculated to be 13.5, 19.5 and 16.5, respectively.

The available data indicate that the nitrophenols are not expected to bioaccumulate strongly in the aquatic environment.

2.2. AIR

The atmospheric chemical removal processes include reaction with hydroxyl radicals, reaction with other radicals, reaction with ozone and photolytic transformations (Cupitt, 1980). Reaction rate constants were not found for any of these reactions; however, Atkinson (1985) reported the rate constant for the reaction of hydroxyl radicals with 2-nitrophenol to be 0.9×10^{-12} cm^3/molecule-sec. Assuming an average atmospheric •OH concentration of 10^6 molecules/cm^3, the calculated half-life for 2-nitrophenol due to •OH reaction is 9 days. This suggests that reaction of the nitrophenols with •OH in the atmosphere may be significant.

As noted in Section 2.1.3., the UV spectra for the nitrophenols in aqueous solution display considerable absorption in the environmentally significant range >290 nm; considerable absorption is also exhibited in a methanol solution (Sadtler, 1960). The data also indicate that 4-nitrophenol undergoes significant environmental photolysis in aqueous solution. This suggests that 4-nitrophenol is likely to undergo significant direct photolysis in the atmosphere. While no data are available for 2- and 3-nitrophenol, direct environmental photolysis of these isomers is also possible.

The physical atmospheric removal processes include dissolution (wet deposition), adsorption on aerosol particles and dry deposition (Cupitt,

1980). The dissolution half-life equation developed by Cupitt (1980) suggests that the nitrophenols may experience an atmospheric removal half-life of ≤3 weeks due to rainfall. 4-Nitrophenol has been detected in ambient rain water (Nojima et al., 1976).

Adsorption on aerosol particles is a reasonable vapor phase removal mechanism only for materials with a saturation vapor pressure of $\leq 10^{-7}$ mm Hg (Cupitt, 1980), which suggests that this mechanism is not important for the nitrophenols; however, Nojima et al. (1983) detected both 2- and 4-nitrophenol in particulates collected over Yokohama, Japan.

2.3. SOIL

2.3.1. **Microbial Degradation.** The following microbial data are in addition to the data presented in Section 2.1.4., but are primarily specific to soil microorganisms.

Zeyer and Kearney (1984) observed that Pseudomonas putida sp., isolated from soil, was able to use 2- and 3-nitrophenol as sole sources of carbon and nitrogen; the 2-nitrophenol was metabolized to catechol and nitrite.

Sudhakar-Barik and Sethunathan (1978) examined the degeneration of the three nitrophenols in flooded alluvial and Pokkali (acid sulfate) soils under laboratory conditions; in 10 days of incubation, a minium of 50% of each nitrophenol had been degraded in both soils. When the soil was additionally inoculated with a parathion-enrichment culture, degradation of the nitrophenols occurred at a significantly faster rate. Sudhakar-Barik et al. (1978) reported that Pseudomonas sp. ATCC29354, isolated from parathion-amended flooded soil, converted 4-nitrophenol to 4-nitrocatechol. Sudhakar-Barik et al. (1976) isolated Pseudomonas sp. and Bacillus sp. from parathion-amended flooded soil and found that they decomposed 4-nitrophenol to CO_2 and nitrite endproducts; the Bacillus sp. decomposed 3-nitrophenol to nitrite and phenol, but was unable to degrade 2-nitrophenol.

Washed cell suspensions of a yeast strain, Candida tropicalir, isolated from soil were able to oxidize the three nitrophenols (Neujahr et al., 1974). Raymond and Alexander (1971) isolated a bacterium from a silt loam soil and found that it was able to use 4-nitrophenol as a carbon and energy source with metabolism to 4-nitrocatechol and nitrite; cells grown on 4-nitrophenol oxidized 3-nitrophenol to nitrohydroquinone. Neujahr and Varga (1970) observed that cell-free preparations of the yeast strain, Trichosporon cutaneum, were able to oxidize the three nitrophenols.

Alexander and Lustigman (1966) examined the biodegradation of the three nitrophenols (sole carbon source) in a mineral salts medium to which a suspension of Niagara silt loam soil was added as inoculum. The 3- and 4-nitrophenols degraded in 4 and 16 days, respectively, while the 2-nitrophenol had not degraded completely after 64 days. Doxtader and Alexander (1966) found that soil bacteria, Actinomycetes, and fungi produced nitrite when using 2- and 3-nitrophenol as sources. Tabak et al. (1964) obtained organisms from garden soil, compost, river mud and waste lagoon sediment and used a mineral salts medium inoculated with the microbes to determine that 95% of the three nitrophenols (300 ppm) were degraded in 3-6 days.

2.3.2. Chemical Degradation. Pertinent data regarding the chemical degradation of nitrophenols in soil were not located in the available literature as cited in the Appendix.

2.3.3. Photolysis. Freitag et al. (1982) examined the photolysis of 4-nitrophenol by adsorbing 80 ng of the compound/g of silica gel medium and then irradiating the medium with 290 nm light; after 17 hours of irradiation, 33.1% of the nitrophenol was photolyzed to CO_2.

As reported in Section 2.1.3., the UV spectra for the nitrophenols show considerable absorption at >290 nm. This fact combined with the photomineralization data of Freitag et al. (1982) suggest that some photolysis of nitrophenols in soil may occur.

2.3.4. Leaching -- Adsorption. Boyd (1982) measured the K_{oc} for the three nitrophenols in a clay loam soil of 5.10% organic matter content and pH 5.7; the K_{oc} values for 2-, 3- and 4-nitrophenol were 113.52, 52.83 and 55.25, respectively.

Artiola-Fortuny and Fuller (1982) measured the adsorption of 4-nitrophenol in five different clay soils with organic contents varying from 0.3-0.9%. From the isotherms produced, the Freundlich's Constant (at 50 ppm concentration) can be used to determine K_{oc} values of 133-400 for the five clay soils.

Wilson and Smith (1981) packed a soil column with sandy soil (>90% sandy; <0.1% organic content) and added 15 cm/day of water containing 1 ppm nitrophenol (isomer not specified). Nitrophenol was not detected in the column effluent; however, when the water was poisoned with sodium azide, >80% of the added nitrophenol was found in the column effluent. The authors suggested that microbial degradation in the column was occurring rapidly enough to prevent leaching when the water was not poisoned.

Saltzman and Yariv (1975) found that 4-nitrophenol is so tightly sorbed to montmorillonite, that it could not be desorbed even under reduced pressure.

The K_{oc} value of an organic compound can be predicted from Equation 2-3, using WS, (Kenaga and Goring, 1978):

$$\log K_{oc} = 3.64 - 0.55 \log WS \text{ (in ppm)} \qquad (2\text{-}3)$$

For 2-, 3- and 4-nitrophenol, the K_{oc} values are calculated to be 65, 23 and 21, respectively. K_{oc} values can be predicted from the K_{ow} value using Equation 2-4 (Kenaga and Goring, 1978):

$$\log K_{oc} = 0.544 \log K_{ow} + 1.377 \qquad (2\text{-}4)$$

For 2-, 3- and 4-nitrophenol, the K_{oc} values are calculated to be 224, 292 and 261, respectively. The molecular topology and activity-structure relationship analysis method reported by Sabljic (1984) suggests that the nitrophenols will have a K_{oc} value of ~1000.

K_{oc} values of 150-500 indicate moderate soil mobility, while values of 1000 indicate low mobility. This suggests that the nitrophenols may be susceptible to moderate leaching in most soil types; however, specific types of clay soils may strongly adsorb the nitrophenols.

2.3.5. Volatilization. Pertinent data regarding volatilization of the nitrophenols from soil were not located in the available literature as cited in the Appendix. Nevertheless, a laboratory study with an environmental test system using ^{14}C-labeled (ring carbon) 4-nitrophenol, Figge et al (1983) reported 20.9, 41.9 and 37.2% of the overall radioactivity in the air, soil and plant phase, 30 days following its application. Of the 20.9% radioactivity detected in the air, only 1.7% was not attributable to $^{14}CO_2$. In the case of 2-nitrophenol, the percent of radioactivity detected in air, soil and plant phase was 55.2, 30.5 and 14.2%, respectively. Of the overall 55.2% radioactivity detected in the air, ~45.3% was not attributable to $^{14}CO_2$. Very little radioactivity (0.02-0.05% of the total) was detected in the percolating water from the application of both 2-nitrophenol and 4-nitrophenol to the environmental test system.

2.3.6. Persistence. In a model soil ecosystem study, Figge et al. (1983) measured the 4-nitrophenol decay rate constant to be 0.105/day; this can be used to calculate a half-life of 6.6 days.

Persistence studies under field conditions were not located in the available literature ascited in the Appendix.

2.4. SUMMARY

The important removal processes for nitrophenols in the aquatic environment appear to be photolysis, microbial degradation and oxidation resulting from sunlight-induced radicals. The combination of these processes suggests that the nitrophenols are not likely to be persistent aquatic compounds. The nitrophenols are not expected to be strongly bioaccumulated.

In the atmosphere, reaction with hydroxyl radicals and direct photolysis may be significant removal processes for nitrophenols; removal via rainfall also may be important.

Soil microorganisms are capable of degrading the nitrophenols; leaching seems to depend on the specific kinds of soil.

3. EXPOSURE

3.1. WATER

According to Cole et al. (1984), storm-water runoff was collected in different cities (15 cities reporting) and analyzed for priority pollutants. 2-Nitrophenol was not detected; however, 4-nitrophenol was detected in runoff from 4 cities (Long Island, NY; Washington, DC; Little Rock, AR; Eugene, OR) at concentrations ranging from 1-19 µg/ℓ.

Young et al. (1983) identified concentrations of <10 µg/ℓ of 4-nitrophenol in primary and secondary effluents from a Los Angeles, CA municipal wastewater treatment plant. Ellis et al (1982) also qualitatively detected 3- or 4-nitrophenol (not separated) and 2-nitrophenol in a treated effluent from a Sangil, IL water treatment plant. Bedient et al. (1984) detected 3-nitrophenol in shallow groundwater beneath a creosote waste site in Conroe, TX at concentrations ranging from 0-43 µg/ℓ. Shackelford and Keith (1976) reported that 2-nitrophenol had been detected in river water and in effluents from chemical plants, 3-nitrophenol was detected in effluent water from a chemical plant in Newport, TN, and 4-nitrophenol was detected in effluent water from a chemical plant in Mt. Pleasant, TN and in effluent from a pesticide plant.

In addition to exposure resulting from direct anthropogenic sources, 4-nitrophenol may be exposed to the aquatic environment as a result of its production from the degradation of other compounds. 4-Nitrophenol is produced as a metabolite by the microbial and hydrolytic decomposition of the pesticides parathion, methyl parathion and fluorodifen (Badawy and El-Dib, 1984; Schultz, 1983; Mitra and Vaidyanathan, 1982; Sudhakar-Barik et al., 1979; Daughton and Hsieh, 1977; Faust, 1975; Tewfik and Hamdi, 1975).

The gross analyses of data available from the U.S. EPA STORET Data Base for 2-nitrophenol and 4-nitrophenol are reported in Tables 3-1 and 3-2, respectively.

3.2. FOOD

Reports of nitrophenol residues in or on ready-to-eat foods were not located in the available literature as cited in the Appendix; however, Archer (1974) detected 4-nitrophenol residues on spinach that had been treated with parathion insecticides.

3.3. INHALATION

Nojima et al. (1983) detected 2- and 4-nitrophenol in atmospheric particulates collected over Yokohama, Japan. Nojima et al. (1976) demonstrated in smog chamber tests that when either benzene or toluene is exposed to UV radiation in the presence of nitrogen monoxide, 2- and 4-nitrophenol are formed. This mechanism may result in ambient atmospheric exposures of the compound.

3.4. DERMAL

Pertinent data regarding dermal exposure to the nitrophenols were not located in the available literature as cited in the Appendix.

TABLE 3-1

U.S. EPA STORET Data for 2-Nitrophenol

Concentration	Water (µg/ℓ)	Sediment (µg/kg)	Fish Tissue (mg/kg)
Number of samples analyzed	4,784	834	580
Maximum	250,000	190,000	50.0
Minimum	0	0	0
Mean	158.3	2,347.7	2.86

TABLE 3-2

U.S. EPA STORET Data for 4-Nitrophenol

Concentration	Water (µg/ℓ)	Sediment (µg/kg)	Fish Tissue (mg/kg)
Number of samples analyzed	4,795	827	551
Maximum	506,655	190,000	50
Minimum	0	0	0
Mean	333.8	2,965	5

4. PHARAMACOKINETICS

4.1. ABSORPTION

Pertinent data regarding the absorption of 2-nitrophenol, 3-nitrophenol or 4-nitrophenol after oral administration or inhalation of these compounds were not located in the available literature as cited in the Appendix. In addition, pertinent data regarding the dermal absorption of 2-nitrophenol or 3-nitrophenol were not located in the available literature as cited in the Appendix.

A dose of 357 µg (40.1 µg/m²) of ^{14}C-labeled 4-nitrophenol was applied dermally to three male New Zealand rabbits over a 7-day period. The reported recovery of ~35% of the radioactivity from the urine indicates that 4-nitrophenol was absorbed through the skin; an additional 0.53% of the applied radioactivity was recovered from the feces of the same three rabbits. Snodgrass (1983) reported that 53% of the applied radioactive dose remained unabsorbed at the site of application at the end of the 7-day experiment.

In a later study, a dose of 714 µ/g (µg/cm²) ^{14}C-labeled 4-nitrophenol was applied dermally to three male beagle dogs, over a 7-day period. The reported recovery of ~11% of the radioactivity from the urine indicated that 4-nitrophenol was absorbed through the skin; <0.5% of the applied radioactivity was recovered from the feces of the same three dogs. Snodgrass (1984) reported that ?6% of the applied radioactive dose remained unabsorbed at the site of application at the end of the 7-day experiment.

4.2. DISTRIBUTION

Pertinent data regarding the distribution of 2- and 3-nitrophenol were not located in the available literature as cited in the Appendix. Radioactive label was not detected in specimens from the liver, lung, kidney,

spleen, heart, brain, adrenal gland, urinary bladder, muscle, bone, fat, thyroid gland, testes, bone marrow or bile of three male New Zealand rabbits 7 days after dermal application or intravenous injection of 357 µg of ^{14}C-labeled 4-nitrophenol, nor was it detected in specimens from three male beagle dogs 7 days after dermal application or intravenous injection of 714 µg of ^{14}C-labeled 4-nitrophenol (Snodgrass, 1983). Skin specimens from one or two dogs contained <5 ppb of ^{14}C-labeled 4-nitrophenol; the route of administration for the dogs with positive skin samples was not reported (Snodgrass, 1984).

4.3. METABOLISM

Robinson et al. (1951) reported that the major metabolites of 2-, 3- and 4-nitrophenol are glucuronide and sulfate conjugates. Additional pertinent data regarding the metabolism of 2- or 3-nitrophenol were not located in the available literature as cited in the Appendix.

Groups of three or four male Wistar rats (200-350 g) were injected in the femoral vein with 1.6, 4.0 or 8.0 mg/kg bw of 4-nitrophenol (Machida et al., 1982). Within 1 minute after dosing, 4-nitrophenyl glucuronide and 4-nitrophenyl sulfate were detected in the plasma by reversed-phase HPLC. These investigators concluded from in vitro experiments that the rate of 4-nitrophenol glucuronidation was highest in the liver (308±18 nmole/tissue/minute) followed by kidney (79±2.3 nmol/tissue/minute), lung (40.8±5.5 nmol/tissue/minute) and small intestine (21.0±6.3 nmol/tissue/minute) and that sulfonation of 4-nitrophenol occurred almost exclusively in the liver. Schmidt-Sonnenschein (1977) reported that 4-nitrophenol sulfate and 4-nitrophenyl glucuronide (water soluble metabolites) were identified in the

kidneys of rats 24 hours after they received 2.7-3.5 mg/kg bw of 4-nitrophenol (route unspecified). Tremaine et al. (1984) reported that 4-nitrophenol glucuronate and 4-nitrophenyl sulfate were identified as metabolites in the kidneys of four rats perfused with 1600-2118 nmol/minute/kg bw of radioactive 4-nitrophenol (Section 4.4.).

In vitro studies with skin and liver cells indicated that 4-nitrophenyl glucuronide and 4-nitrophenyl sulfate are the major conjugates of 4-nitrophenol (Tonda and Hirata, 1983; Moldeus et al., 1976; Rugstad and Dybing, 1974, 1975).

4.4. EXCRETION

Robinson et al. (1951) reported that rabbits excrete 2-, 3- and 4-nitrophenol mainly via the urine, and that excretion of all three isomers was, in effect, completed within 24 hours after dosing (route of administration not specified). Additional pertinent data regarding the excretion of 2- and 3-nitrophenol were not located in the available literature as cited in the Appendix.

4-Nitrophenol was eliminated from the blood within 2 hours after intraperitoneal injection in mice, rabbits, guinea pigs, rats and monkeys; the rate of elimination in monkeys was comparable following intraperitoneal injection and oral administration (Robinson et al., 1951). Lawford et al. (1954) reported that 4-nitrophenol was eliminated from the blood of monkeys within 5 hours of either an oral dose or intraperitoneal injection of 20 mg/kg bw.

According to Snodgrass (1984), the half-life of ^{14}C-labeled 4-nitrophenol in the circulating blood of dogs, after intravenous injection, was ~15 minutes, and radioactivity was nearly undetectable in the blood 4 hours after dosing (Snodgrass, 1984).

Machida et al. (1982) injected the femoral veins in groups of three or four rats with 1.6, 4.0 or 8.0 mg/kg bw of 4-nitrophenol (see Section 4.3.) and collected the urine and bile for 24 hours. As indicated in Table 4-1, analysis with reversed phase HPLC revealed that 71.7-99.0% of the administered dose was excreted in the urine as either 4-nitrophenyl glucuronide or 4-nitrophenyl sulfate within 24 hours of dosing. The amount of unchanged 4-nitrophenol identified increased directly with increasing intravenous doses of 4-nitrophenol.

Gessner and Hamada (1974) reported that radioactive 4-nitrophenyl glucuronate, identified in the bile, comprised ~20% of the administered dose of ^{14}C-labeled 4-nitrophenol in perfused rat livers within 70 minutes of dosing.

Four rats were infused via the jugular vein with 1600-2118 nmol/minute/kg bw of ^{14}C-labeled 4-nitrophenol for 90 minutes, and four consecutive 15-minute urine samples and midpoint blood samples were collected (Tremaine et al., 1984). The 4-nitrophenyl sulfate and 4-nitrophenyl glucuronide that was synthesized in the kidney and excreted directly into the urine without entering the systemic circulation was designated the nephrogenic conjugate. The 4-nitrophenyl sulfate and 4-nitrophenyl glucuronide that entered the systemic circulation was designated the non-nephrogenic conjugate, regardless of where it was synthesized. Unchanged ^{14}C-labeled 4-nitrophenol was not detected in the urine. Of the infused radioactivity, ~75.2$\pm$2.5% was recovered from the urine during the experiment.

4-Nitrophenyl sulfate and 4-nitrophenyl glucuronide comprised 99% of the radioactive compounds recovered from the urine. Of the ~20% of the radioactivity that was excreted directly into the urine, half was 4-nitrophenyl

TABLE 4-1

Cumulative Percentages of the Dose Excreted in Urine and Bile as p-Nitrophenol, and as its Glucuronide and Sulfate, in the 24 Hours Following Femoral Vein Administration of 4-Nitrophenol to Rats[a,b]

Intravenous Dose (mg/kg)	4-Nitrophenol in Urine	Glucoronide in Urine	Sulfate in Urine	Glucuronide in Bile
1.6	1.8 ± 3.1	37.4 ± 0.8	61.6 ± 4.4	6.2 ± 3.7
4	2.2 ± 0.6	41.0 ± 3.8	40.0 ± 3.7	11.1 ± 4.0
8	7.4 ± 5.8	41.0 ± 8.8	30.7 ± 8.6	7.9 ± 3.9

[a]Source: Machida et al., 1982

[b]Each value is the mean ± SD of four (8 mg/kg) and three (1.6 and 4 mg/kg) rats.

sulfate and half was 4-nitrophenyl glucuronide. Bile was collected continuously during the experiment from one of the infused rats and contained ~0.9% of the administered radioactivity. Tremaine et al. (1984) suggested that biliary excretion was not a significant route of excretion in their experiment.

Injection of 357 µg of ^{14}C-labeled 4-nitrophenol into the marginal ear vein of three male New Zealand rabbits resulted in 79% of the administered radioactivity being recovered from the urine and ≤1% recovered from the feces within 7 days of dosing (Snodgrass, 1983). Of the recovered radioactivity, >96% was excreted in the urine and feces within 24 hours of dosing.

Injection of 714 µg of ^{14}C-labeled 4-nitrophenol into the cephalic vein of three male Beagle dogs resulted in 95% of the administered radioactivity being recovered from the urine and ≤1% recovered from the feces within 7 days of dosing (Snodgrass, 1984). Of the recovered radioactivity, >96% was excreted in the urine and feces within 24 hours of dosing.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of 3-nitrophenol were not located in the available literature as cited in the Appendix.

In an experiment designed to evaluate the ability to promote skin tumorigenesis, one drop (~25 µl) of a 20% solution of 2- or 4-nitrophenol in dioxane was applied twice weekly to the backs of 31 mice for 12 weeks (Tables 5-1 and 5-2). Although one mouse died during each experiment from an unreported cause, none of the mice treated with 2- or 4-nitrophenol showed any evidence of skin tumors at the end of 12 weeks. No chemical initiator was applied to the mouse skin prior to the application of 2- or 4-nitrophenol (Boutwell and Bosch, 1959).

4-Nitrophenol has been scheduled for toxicity testing by means of a skin painting assay in mice (NTP, 1984).

5.2. MUTAGENICITY

As indicated in Table 5-3, 2-nitrophenol did not increase the rate of reverse mutation in Salmonella typhimurium strains TA98, TA100, TA1535 or TA1537, or in Escherichia coli either in the presence or absence of metabolic activation (Taylor, 1979a; Chiu et al., 1978; Szybalski, 1958; Suzuki et al., 1983; Haworth, 1983).

As indicated in Table 5-4, Taylor (1979b) reported that 3-nitrophenol increased the frequency of reverse mutations in S. typhimurium strain TA98 without metabolic activation; however, Suzuki et al. (1983) reported that 3-nitrophenol did not increase the frequency of reverse mutations in S. typhimurium strain TA98. In the presence of metabolic activation, 3-nitrophenol increased the frequency of reverse mutations in S. typhimurium strains TA100 and TA1535 but did not increase the frequency of reverse

TABLE 5-1

Animal*

Agent: 2-Nitrophenol

Exposure Route	Species/ Strain	Sex	Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
Dermal	mice/ Sutter	F	25 µl (twice weekly)	12 weeks	12 weeks	NR	dioxane	skin	no effect	no effect

QUALITY OF EVIDENCE

Strengths of Study: 30 of 31 mice survived the experiment.

Weakness of Study: The study was designed to test the promoting ability of 2-nitrophenol but no initiator was used.

Overall Adequacy: Inadequate

*Source: Boutwell and Bosch, 1959

NR = Not reported

TABLE 5-2

Animal*

Agent: 4-Nitrophenol

Exposure Route	Species/ Strain	Sex	Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
Dermal	mice/ Sutter	F	25 µL (twice weekly)	12 weeks	12 weeks	NR	dioxane	skin	no effect	no effect

QUALITY OF EVIDENCE

Strengths of Study: 30 of 31 mice survived the experiment

Weakness of Study: The study was designed to test the promoting ability of 4-nitrophenol but no initiator was used.

Overall Adequacy: Inadequate

*Source: Boutwell and Bosch, 1959

NR - Not reported

TABLE 5-3

Mutagenicity of 2-Nitrophenol

Assay	Indicator Organism/Strain	Application Method	Concentration/ Dose	Metabolic Activation	Response	Comments	Reference
Reverse mutation	S. typhimurium/ TA98 TA100 TA1535 TA1537	NR	NR	+/-	-/-	NC	Taylor, 1979a
Reverse mutation	S. typhimurium/ TA98 TA100 TA1535 TA1537	plate incorporation	0.1-10 µmol	-	-	NC	Chiu et al., 1978
Reverse mutation	E. coli/ Sd-4-73	spot test	small crystal	-	-	The small crystal of 2-nitrophenol was either placed directly on the agar or on a small filter-paper disk resting on the agar	Szybalski, 1958
Reverse mutation	S. typhimurium/ TA98 TA100	plate incorporation	<100 µg/plate	+/- -	-/- -	The mutagenicity of 2-nitrophenol was not tested in strain TA100 in the presence of S-9. Norharman did not affect the mutagenicity of 2-nitrophenol in strain TA98.	Suzuki et al., 1983
Reverse mutation	S. typhimurium/ TA98 TA100 TA1535 TA1537	plate incorporation	0.0-1000 µg/plate	+/- +/- +/- +/-	-/- -/- -/- -/-	NC	Haworth et al., 1983

NR = Not reported; NC = no comment

0678p 09/20/85

TABLE 5-4

Mutagenicity of 3-Nitrophenol

Assay	Indicator Organism/Strain	Application Method	Concentration/ Dose	Metabolic Activation	Response	Comments	Reference
Reverse mutation	S. typhimurium/ TA98	NR	NR	-	+	NC	Taylor, 1979b
	TA100			+	+		
	TA1535			+	+		
	TA1537			+/-	-/-		
Reverse mutation	E. coli/ Sd-4-73	spot test	small crystal	-	-	The small crystal of 3-nitrophenol was either placed directly on the agar or on a small filter-paper disk resting on the agar.	Szybalski, 1958
Reverse mutation	S. typhimurium/ TA100	plate incorporation	<100 µg/plate	+/-	-/-	The mutagenicity of 3-nitrophenol was not tested in strain TA100 in the presence of S-9. Norharmon did not affect the mutagenicity of 3-nitrophenol in strain TA98.	Suzuki et al., 1983
				-	-		

NR = Not reported; NC = no comment

mutations in S. typhimurium strain TA1537, regardless of the presence or absence of metabolic activation (Taylor, 1979b). In the absence of metabolic activation, 3-nitrophenol did not increase the frequency of reverse mutations in E. coli (Szybalski, 1958).

As indicated in Table 5-5, 4-nitrophenol did not increase the frequency of reverse mutations in S. typhymurium strains TA98, TA100, TA1535, TA1537, TA1538, D3052, C3075 or G46 (McCann et al., 1975; Bracha, 1979; Taylor, 1979a; Suzuki et al., 1983; Probst et al., 1981; Haworth et al., 1983) or in E. coli strains Sd-4-73, WP2, WP2uvrA$^-$, K12 env AuvrB or K12 env AuvrB (λc2Its 857) regardless of the presence or absence of metabolic activation (Szybalski, 1958; Ho and Ho, 1981; Probst et al., 1981). In addition, 4-nitrophenol did not increase the frequency of forward mutations in mouse lymphoma cells incubated with or without metabolic activators (Amacher and Turner, 1982; Oberly et al., 1984). A summarized report (Fahrig, 1974) indicated that 4-nitrophenol did not increase the frequency of forward mutations in E. coli or Serratia marcescens, or of recessive lethal mutations in Drosophila melanogaster. Based on his own research, Fahrig (1974) reported that 4-nitrophenol increased the frequency of mitotic gene conversion in Saccharomyces cerevisiae. An increase in the frequency of mitotic gene conversion is presumably indicative of the occurrence of single-strand breaks in the DNA molecule (Fahrig, 1974). In an experiment designed to test the effect of various compounds on DNA repair, confluent cultures of human fibroblasts were cultivated with N-acetoxy-2-acetylaminofluorene to induce DNA damage (Poirier et al., 1975). 4-Nitrophenol inhibited both repair and replicative DNA synthesis at a concentration of 10^3 µM (1 mM). von Propping et al. (1973) and Buselmaier et al. (1972, 1973) reported that 4-nitrophenol produced negative results in an in vitro assay and a host-mediated assay using S. typhimurium and S. marcescens.

TABLE 5-5

Mutagenicity of 4-Nitrophenol

Assay	Indicator Organism/Strain	Application Method	Concentration/ Dose	Metabolic Activation	Response	Comments	Reference
Reverse mutation	S.typhimurium/						
	TA98	NR	NR	+/-	-/-	NC	McCann et al., 1975; Taylor, 1979a; Bracha, 1979
	TA100	NR	NR	+/-	-/-	NC	
	TA1535	NR	NR	+/-	-/-	NC	
	TA1537	NR	NR	+/-	-/-	NC	
Reverse mutation	E. coli/						
	Sd-4-73	spot test	small crystal	-	-	The small crystal of 4-nitrophenol was either placed directly on the agar or on a small filter-paper disk resting on the agar.	Szybalski, 1958
Reverse mutation	S. typhimurium/						
	TA98	plate incorporation	≤100 µg/plate	+/-	-/-	The mutagenicity of 4-nitrophenol was not tested in strain TA100 in the presence of S-9. Norharman did not affect the mutagenicity of 4-nitrophenol in strain TA98.	Suzuki et al., 1983
	TA100			-	-		
Reverse mutation	S. typhimurium/						
	TA98	same as above	NR	+/-	-/-	NC	Probst et al., 1981
	TA100		NR	+/-	-/-	NC	
	TA1532		NR	+/-	-/-	NC	
	TA1537		NR	+/-	-/-	NC	
	TA1538		NR	+/-	-/-	NC	
	C3075		NR	+/-	-/-	NC	
	D3052		NR	+/-	-/-	NC	
	G46		NR	+/-	-/-	NC	
Reverse mutation	E. coli/						
	WP2	same as above	NR	+/-	-/-	NC	Probst et al., 1981
	WP2uvrA		NR	+/-	-/-	NC	

0678p

09/20/85

TABLE 5-5 (cont.)

Assay	Indicator Organism/Strain	Application Method	Concentration/ Dose	Metabolic Activation	Response	Comments	Reference
Reverse mutation	S. typhimurium/ TA98	same as above	0.0-1000 µg/plate	+/-	-/-	NC	Haworth et al., 1983
	TA100			+/-	-/-	NC	
	TA1535			+/-	-/-	NC	
	TA1537			+/-	-/-	NC	
Prophage induction test	E. coli/ K12 env AuvrB	plate incorporation	<0.75 mg/mL	+	-	NC	Ho and Ho, 1981
	K12 env AuvrB (λc2Its857)			+	-	NC	
Forward mutation	mouse lymphoma cells/ L5178YTK +/-	same as above	58.0-782.0 µg/L	+	-	The lymphoma cells were cultivated in soft agar containing the chemical for a period of 3 hours.	Amacher and Turner, 1982
Forward mutation	mouse lymphoma cells/ L5178YTK +/-	same as above	700-1500 µg/L or 0.1-30 µg/L (see comment)	+/-	-/-	The higher range of concentrations was used without metabolic activation, while the lower range was used in the presence of S-9.	Oberly et al., 1984
Unscheduled DNA synthesis	rat hepatocytes/ primary culture	medium incorporation	≤100 nmol/mL	-	-	The cells were cultivated with 4-nitrophenol.	Probst et al., 1981

NR = Not reported

0678p

09/20/85

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of 2-, 3- or 4-nitrophenol were not located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of 2-, 3- or 4-nitrophenol were not located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Pertinent data regarding the chronic and/or subchronic toxicity of 2-, 3- or 4-nitrophenol were not located in the available literature as cited in the Appendix.

5.6. OTHER RELEVANT INFORMATION

The acute oral toxicity of 2-, 3- and 4-nitrophenol is reported in Table 5-6. Pertinent data regarding the acute inhalation or dermal toxicity of the mononitrophenols were not located in the available literature as cited in the Appendix.

von Oettingen (1941) reported methemoglobin formation in cats treated with 2-nitrophenol, and Grant (1959) reported a variable amount of methemoglobin formation in rats treated intraperitoneally with 60-120 mg of 2-nitrophenol.

Three guinea pigs maintained on a vitamin C deficient diet and treated intraperitoneally with daily injections of 2.5 mg of 2-nitrophenol for 20 days did not develop cataracts (Ogino and Yasukura, 1957). Similarly, no cataracts developed in 7-day-old chicks treated with 2-nitrophenol (Dietrich and Buetner, 1946).

Cameron (1958) reported that the body temperature of rats decreased but there was no change in the rate of oxygen consumption or carbon dioxide

TABLE 5-6

Acute Toxicity of Orally Administered Mononitrophenols

Isomer	Species	LD_{50} (mg/kg)	Reference
2-Nitrophenol	rat	2830	Vernot et al., 1977
	mouse	1300	
3-Nitrophenol	rat	930	Vernot et al., 1977
	mouse	1410	
4-Nitrophenol	rat	620	Vernot et al., 1977
	rat	350	Fairchild, 1977
	mouse	470	Vernot et al., 1977

output after an intraperitoneal injection of ~120 mg of 2-nitrophenol. No change in body temperature or bi e secretion was observed in dogs injected intravenously with 5-6 mg/kg of 2-nitrophenol (Pugh and Stone, 1968). An intraperitoneal injection of ~60-120 mg of 2-nitrophenol in rats resulted in a decreased tidal volume and increased respiratory rate and minute ventilatory volume (Grant, 1959). von Oettingen (1941) reported an initial stimulation of respiration after treatment with 2-nitrophenol, followed by depression in cases of fatal poisoning. An intragastric dose of 0.8 g/kg bw 2-nitrophenol to rats uncoupled oxidative phosphorylation, increased liver NADH, and decreased ATP content and cytochrome oxidase activity (Kolodub and Vasilenko, 1976).

The platelet count in rats increased significantly after intraperitoneal injection of 0.1 and 1 mg/kg bw of 2-nitrophenol (Gabor et al., 1962). Motais et al. (1978) reported that 2-nitrophenol inhibited chloride transport in the erythrocyte plasma membrane.

3-Nitrophenol is reported to be a metabolite of nitrobenzene in rats, and the glucuronide of 3-nitrophenol is reported to be a metabolite of nitrobenzene in mice (Rickert et al., 1983).

3-Nitrophenol at a dose of 20-45 mg per rat decreased the tidal volume but increased the minute volume and rate of respiration; no increase in methemoglobin was reported (Grant, 1959). There was a significant decrease in body temperature in rats treated with 45 mg of 4-nitrophenol, but no effect on carbon dioxide was reported (Cameron, 1958).

von Oettingen (1941) reported that 4-nitrophenol treatment resulted in methemoglobin formation in cats, but this observation was not confirmed in rats treated with 7-12 mg of 4-nitrophenol (Grant, 1959). Smith et al. (1967), however, reported that 4-aminophenol, the reduced form of 4-nitrophenol, produced methemoglobin formation in female mice.

Two of three guinea pigs treated intraperitoneally with 2.5 mg/day of 4-nitrophenol for 20 days and maintained on a vitamin C deficient diet developed cataracts on days 7 and 11 of the experiment (Ogino and Yasukura, 1957). The number of guinea pigs with cataracts in control groups (i.e., on vitamin C deficient diets without 4-nitrophenol treatment or on vitamin C sufficient diets) was not reported. 4-Nitrophenol did not cause cataracts in 7-day-old chicks, although 2,4-dinitrophenol did (Dietrich and Beutner, 1946).

Lawford et al. (1954) reported that the body temperature decreased but there was no change in the amount of oxygen consumed in rats treated with ~66 mg/kg of 4-nitrophenol administered intraperitoneally. Cameron (1958) confirmed the decrease in body temperature accompanied by increased carbon dioxide exhalation, but did not note a change in oxygen consumption in rats injected intraperitoneally with 12 mg of 4-nitrophenol. A dose of 7-12 mg was reported to cause increased respiratory rates and increased minute ventilation and tidal volumes in rats (Grant, 1959). Increased respiration, followed by depressed respiration in cases of fatal poisoning, was reported by von Oettingen (1941).

In dogs, both the aortic and carotid chemoreceptors were stimulated by 4-nitrophenol (Shen, 1962). A large dose (500 mg/kg) of 4-nitrophenol administered intraperitoneally caused a fatal drop in body temperature in dogs (von Oettingen, 1941), but a smaller dose (5-6 mg/kg) administered intravenously had no effect on the body temperature or bile secretion of dogs (Pugh and Stone, 1968).

An intragastric dose of 0.11 g/kg 4-nitrophenol in rats uncoupled oxidative phosphorylation and increased liver NADH content, decreased ATP content and inhibited cytochrome oxidase (Kolodub and Vasilenko, 1976). Motais et al. (1978) included both 2-nitrophenol and 4-nitrophenol on their list of

oxidative phosphorylation uncouplers and suggested that inhibition of chloride transport in red blood cells was correlated with the ability of a compound to uncouple oxidative phosphorylation.

4-Nitrophenol has been reported to be one of the metabolites of a number of compounds. 4-Nitrophenol was a metabolite of parathion in cultivated HeLa cells and human skin fibroblasts (Litterst and Lichtenstein, 1971), of paraoxon [O,O-diethyl-O-(4-nitrophenyl) phosphate] when incubated with mouse liver microsomes (Sultatos and Murphy, 1983), of butyl 4-nitrophenyl ether after oral administration (~300 mg/kg bw) to rats, mice, guinea pigs and rabbits (Yoshimura et al., 1967), of nitrobenzene in rats and mice (Rickert et al., 1983) and of 4-nitrophenetole when incubated with rat liver microsomes (Joergensen and Johansen, 1983).

Intraperitoneal injection of pregnant rats with cortisol and/or dexamethasone increased the fetal activity of UDP-glucuronyltransferase, an enzyme known to conjugate 4-aminophenol (Wishart and Dutton, 1977). Increased secretion of adrenaline by the perfused rabbit adrenal medulla occurred after treatment with 4-nitrophenol (Sorimachi and Yamagami, 1982).

Gram et al. (1974) reported significantly higher levels of the enzyme used to conjugate 4-nitrophenol, UDP-glucuronyltransferase, in the rabbit liver than in the rabbit lung, where the level of UDP-glucuronyltransferase was reported to be zero. Cuhabra and Fouts (1974) reported sex-linked differences in the activity level of UDP-glucuronyltransferase; UDP-glucuronyltransferase activity was significantly greater in male rabbit livers and in female rabbit kidneys, but there was no difference between male and female rabbit UDP-glucuronyltransferase activity in the gut or in the lung. Strain differences in rats (Yeary and Fleming, 1971), as well as species differences among cattle, sheep, swine and rats (Smith et al., 1984), in

UDP-glucuronyltransferase activity were also reported (Yeary and Fleming, 1971).

Garrett and Lewtas (1983) reported that 4-nitrophenol was moderately toxic to Chinese hamster ovary cells *in vitro*. According to Garrett and Lewtas (1983), a chemical was moderately toxic when a dose in the range of 10-100 µg/mℓ of tissue culture medium produce a 50% reduction in DNA synthesis in the cultivated cells. The development of preimplantation mouse embryos *in vitro* was adversely affected by 4-nitrophenol (Muller et al., 1981). The effect was irreversible when the concentration of 4-nitrophenol in the culture medium was 0.5×10^{-3} M. No effect was seen at a concentration of 10^{-6} M 4-nitrophenol. Although both 4-nitrophenol and x-irradiation induce the formation of micronuclei in cultivated preimplantation mouse embryos, no evidence of synergism was reported when the two treatments were given simultaneously (Muller et al., 1981). Motais et al. (1978) reported that 4-nitrophenol inhibited chloride transport in red blood cells, while Sorimachi and Yamagami (1982) suggested that 4-nitrophenol increased the rate of calcium influx across the plasma membrane.

The nutritional state of the individual has been reported to affect the metabolism of 4-nitrophenol (Sonawane et al., 1983; Reinke et al., 1979, 1981; Thurman et al., 1981).

A Russian study indicated that the mononitrophenols were mildly to moderately toxic to rats and mice treated orally with one-fifth the LD_{50} for 30 days (Vasilenko et al., 1976). In another Russian study, thresholds for "conditioned reflex activity" were reported to be 3 µg/kg 2- and 3-nitrophenol and 1.25 µg/kg for 4-nitrophenol (Makhinya, 1969). Experimental details, including species and duration of exposure, are not provided in the abstract.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

In toxicity tests using rainbow trout, Salmo gairdneri, 4-nitrophenol was administered by intraperitoneal injection, oral intubation or in the ambient water (Hodson et al., 1984). The LD_{50} values determined 96 hours after treatment for intraperitoneal and oral exposure were 47.3 and 61.2 mg/kg 4-nitrophenol, respectively. The 96-hour LC_{50} for 4-nitrophenol in continuous-flowing water was 7.9 mg/ℓ in the rainbow trout.

Using bluegill sunfish, Lepomis macrochirus, as a test species, toxicity tests of 4-nitrophenol were conducted for 96 hours (U.S. EPA, 1978; Buccafusco et al., 1981; LeBlanc, 1984). Various concentrations of 4-nitrophenol were tested to determine LC_{50} values for 24, 48, 72 and 96 hours. The LC_{50} values ranged from 11.46 mg/ℓ for 24 hours to 8.28 mg/ℓ for the longer durations. The 96-hour LC_0 mg/ℓ was 2.2 mg/ℓ 4-nitrophenol (U.S. EPA, 1978). Testing the toxicity of 2-nitrophenol in bluegills, L. machrochirus, Lammering and Burbank (1960) reported 24- and 48-hour LC_{50} values of 66.9 and 46.3-51.6 mg/ℓ, respectively.

Phipps et al. (1981) conducted static and flowthrough toxicity tests of 4-nitrophenol in fathead minnows, Pimephales promelas. The 48-hour LC_{50} value determined under static conditions was 10 mg/ℓ 4-nitrophenol, while 96-hour flowthrough LC_{50} values of 49 and 62 mg/ℓ were reported. Holcombe et al. (1984) reported that the 24-, 48-, 72- and 96-hour LC_{50} values for fathead minnows were 64.6, 54.4, 44.1 and 41.0 mg/ℓ 4-nitrophenol. In the channel catfish, Holcombe et al. (1984) reported an LC_{50} of 15.0 mg/ℓ 4-nitrophenol for all exposure periods (24, 48, 72 and 96 hours).

The 96-hour LC_{50} values of 3-nitrophenol and 4-nitrophenol at various pH levels were determined using guppies, Poecilia reticulata, as test organisms (Saarikoski and Viluksela, 1982). The 96-hour LC_{50} values for 4-nitrophenol were 8.97, 14.19 and 39.19 mg/ℓ, and for 3-nitrophenol were 11.04, 11.84 and 16.76 mg/ℓ, respectively, at pH 6.0, 7.0 and 8.0. Tonogai et al. (1982) reported 24- and 48-hour LC_{50} values of 12.0 and 7.0 mg/ℓ 4-nitrophenol, respectively, in the medaka, Oryzias latipes.

Toxicity testing of 4-nitrophenol in the marine sheepshead minnow, Cyprinodon variegatus, has been conducted by the U.S. EPA (1978), Heitmuller et al. (1981) and LeBlanc (1984). Tests of 96 hours duration were conducted using various concentrations of 4-nitrophenol to determine 24-, 48-, 72- and 96-hour LC_{50} values and a 96-hour LC_0. The 24- and 48-hour LC_{50} values were both 27.7 mg/ℓ, and the 72- and 96-hour LC_{50} values were 27.1 mg/ℓ. The 96-hour LC_0 was reported to be 24.0 mg/ℓ 4-nitrophenol. Ward et al. (1981) reported a 96-hour LC_{50} of 32 mg/ℓ 4-nitrophenol in juvenile sheepshead minnows.

The water flea, Daphnia magna, has been used in toxicity tests of 4-nitrophenol by the U.S. EPA (1978), LeBlanc (1980, 1984), Bringmann and Kuhn (1977), Klein et al. (1984) and Kopperman et al. (1974). Kopperman et al. (1974) determined a 96-hour static LC_{50} of 8.4 mg/ℓ. Mean 24- and 48-hour LC_{50} values reported by the U.S. EPA (1978) and LeBlanc (1980) were 24.4 and 27.0 mg/ℓ, respectively. The higher LC_{50} value at the longer exposure period may indicate evaporative or degradative loss of the 4-nitrophenol. Klein et al. (1984) reported an EC_{50} at 9.8 mg/ℓ (duration and effect not specified) in D. magna. The NOEL concentration determined during toxicity tests in D. magna was 13 mg 4-nitrophenol/mg/ℓ.

Bringmann and Kuhn (1977) reported 24-hour LC_{50} values of 210, 39 and 35 mg/ℓ for 2-, 3- and 4-nitrophenol, respectively, in D. magna. In the freshwater rotifer, Brochionus rubens, a 24-hour LC_{50} value of 6.3 mg/ℓ 4-nitrophenol was determined by Halbach et al. (1983).

The 24-, 48-, 72- and 96-hour LC_{50} values determined in the mysid shrimp, Mysidopsis bahia, were 8.66, 9.89, 7.90 and 7.17 mg/ℓ 4-nitrophenol, respectively (U.S. EPA, 1978; LeBlanc, 1984). The LC_0 was 1.8 mg/ℓ. In the shrimp, Crangon septemspinosa, the 96-hour lethality threshold levels for 2- and 4-nitrophenol were determined to be 32.9 and 26.4 mg/ℓ, respectively (McLeese et al., 1979). In the soft-shelled marine clam, Mya arenaria, the 96-hour lethality threshold was 29.4 mg/ℓ nitrophenol (McLeese et al., 1979).

6.2. CHRONIC AND SUBCHRONIC TOXICITY

The 192-hour (8-day) LC_{50} determined in fathead minnows, P. promelas, was 49-50 mg/ℓ 4-nitrophenol during flowthrough testing (Phipps et al. 1981; Alexander et al., 1983).

Embryo-larval toxicity tests of 4-nitrophenol were conducted using the marine sheepshead minnows, C. variegatus, exposed for 28 days after fertilization (Ward et al., 1981). Hatching success and juvenile mortality were inhibited severely at 4-nitrophenol concentrations of $\geq$16 mg/ℓ (2 and 100%, respectively) but were not different from control levels at concentrations <10 mg/ℓ. The estimated MATC was, therefore, between 10 and 16 mg/ℓ 4-nitrophenol. Exposure of developing larvae to 4-nitrophenol at sublethal levels did not appear to increase the incidence of physical abnormalities (Ward et al., 1981).

Halbach et al. (1983) exposed rotifers, B. rubens, to 4-nitrophenol at 1-20 mg/ℓ for up to 30 days to determine population survival and fertility. At a level of 1 mg 4-nitrophenol/ℓ, no significant change in population viability was observed. Initially, levels of 2-5 mg/ℓ were inhibitory to population growth, but adaptation occurred over several generations so that little effect was evident after 30 days of exposure. Higher levels were severely detrimental to the rotifer populations, causing complete extinction within 10 days (Halbach et al., 1983).

The effect of a 24-hour exposure to 4-nitrophenol at 10 mg/ℓ on the lifespan and reproductive performance of the brine shrimp, Artemia salina, was studied by Grosch (1973). Following the 24-hour exposure at 10 mg/ℓ, the average lifespan of A. salina was reduced from ~50 days to 35-38 days. Reproductive performance was reduced as well. The average numbers of broods and total zygotes were reduced to 5.7 and 1031, respectively, compared to 11.3 and 1828 in controls. Hatching success and larval survival was not affected significantly (Grosch, 1973).

6.3. PLANT EFFECTS

The toxicity threshold levels of 2-, 3- and 4-nitrophenol that retarded cell proliferation in the blue-green algae, Microcystis aeruginosa, after 8 days of incubation were 27, 17 and 56 mg/ℓ, respectively (Bringmann, 1975). In the freshwater green algae, Selenastrum capricornutum, 24-, 48-, 72- and 96-hour EC_{50} values for inhibited chlorophyll production were 4.52, 5.54, 4.53 and 4.19 mg 4-nitrophenol/ℓ, respectively (U.S. EPA, 1978; LeBlanc, 1984). The LC_0 was reported to be <0.3 mg 4-nitrophenol/ℓ. Huang and Gloyna (1967) reported 72-hour EC_{50} values for inhibited chlorophyll synthesis in the green algae, Chlorella pyrenoidosa, of 35, 50 and 25 mg/ℓ for 2-, 3- and 4-nitrophenol. Dedonder and Van

Sumere (1971) reported 50% growth inhibition in Chlorella vulgaris exposed to 6.95 mg 4-nitrophenol/ℓ for 80 hours. The toxicity threshold values for inhibited cell multiplication in Scenedesmus quadricauda following 8 days of exposure were 4.3, 7.6 and 7.4 mg/ℓ for 2-, 3- and 4-nitrophenol, respectively (Bringmann and Kuhn, 1978).

In the marine algae, Skeletonema costatum, the U.S. EPA (1978) determined 24-, 48-, 72- and 96-hour EC_{50} values of 8.45, 6.84, 7.40 and 7.37 mg 4-nitrophenol/ℓ, respectively. The LC_0 was <0.56 mg/ℓ.

6.4. RESIDUE

Call et al. (1980) reported a whole body BCF of 180 for 4-nitrophenol in fathead minnows, P. promelas. Geyer et al. (1981) reported a BCF of 11 for 4-nitrophenol in the algae, Chlorella fusca. Klein et al. (1984) reported a 1-day BCF in agae of 11 and a 3-day BCF of 57 in fish (species not specified).

Young et al. (1983) reported that 4-nitrophenol concentrations were <10 µg/ℓ in a Los Angeles wastewater treatment plant.

6.5. OTHER RELEVANT INFORMATION

Studies on the kinetics of nitrophenols in freshwater fish (Call et al. 1980; Nagel and Urich, 1980) indicate that uptake of nitrophenols is somewhat slow and elimination is rapid. Elimination is primarily through the gills. Elimination of 3-nitrophenol from the frog, Rana temporaria, is rather rapid (being nearly complete within 15 hours), with renal elimination being the primary route (Nagel and Urich, 1981). Slight retention in the gall bladder and gut contents was evident. Elimination of 3-nitrophenol in the crayfish, Astacus leptodactylus, was slower, with elimination not complete by 45 hours (Nagel and Urich, 1981). Elimination through the gills is the primary route in the crayfish. In the lobster, Homarus americanus,

metabolism of 4-nitrophenol is primarily by hepatopancreatic sulfoconjugation (Elmamlouk and Gessner, 1978). Sea urchins, Strongylocentrotus purpuratus, and starfish, Pisaster ochroceus, had excreted 36 and 88% of injected 4-nitrophenol within 8 hours (Landrum and Crosby, 1981).

Laitinen et al. (1982) reported that liver fractions from the splake (Salvelinus fontinalia x Salvelinus namaycush) and lavaret, Coregonus lavaretus, showed increased aryl hydrocarbon hydroxylase, epoxide hydrase, ethoxycoumarin O-deethylase and UDP glucuronosyl transferase activities when treated with 4-nitrophenol. Enzyme activities were higher in the splake.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

In the USSR, drinking water limits of 0.02 mg/ℓ for 4-nitrophenol and 0.06 mg/ℓ for 2-nitrophenol and 3-nitrophenol have been reported (Stofen, 1973).

Other pertinent guidelines and standards for 2-nitrophenol, 3-nitrophenol or 4-nitrophenol including EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, EPA or FDA tolerances for raw agricultural commodities or foods, and ACGIH, NIOSH or OSHA occupational exposure limits were not located in the available literature as cited in the Appendix.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of mononitrophenols were not located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

The application of 2-nitrophenol or 4-nitrophenol to the skin of mice for 12 weeks did not result in the formation of skin tumors within that time period (Boutwell and Bosch, 1959); however, the carcinogenicity of the mononitrophenols has not been studied adequately. Neither 2-nitrophenol nor 4-nitrophenol caused an increased frequency of reverse mutations in bacterial assays in the presence or absence of metabolic activation (McCann et al., 1975; Taylor, 1979a; Chiu et al., 1978; Szybalski, 1958; Suzuki et al., 1983; Bracha, 1979; Probst et al., 1981). In addition, 4-nitrophenol did not increase the frequency of forward mutations in cultivated mammalian cells (Amacher and Turner, 1982; Oberly et al., 1984) or prophage inductions in E. coli (Ho and Ho, 1981). These tests were not performed to evaluate the mutagenicity of 2-nitrophenol. 3-Nitrophenol increased the frequency of reverse mutations in S. typhimurium strain TA98 without metabolic activation and in S. typhimurium strain TA100 and TA1535 only in the presence of metabolic activators (Taylor, 1979b). The results with strain TA98 were not confirmed by Suzuki et al. (1983). Pertinent data regarding the teratogenicity, reproductive effects or chronic toxicity of 2-nitrophenol, 3-nitrophenol or 4-nitrophenol were not located in the available literature as cited in the Appendix. The three isomers of mononitrophenol appear to have different toxicity levels (see Table 5-6), and elicit different effects (see Section 5.6.). Although there were no in vivo teratological or reproductive studies available, 4-nitrophenol adversely affected the development of preimplantation mouse embryos in vitro (Muller et al., 1981). The mononitrophenols appeared to adversely affect metabolism in various species and as measured by various methods (Lawford et al., 1954; Cameron, 1958; Grant,

1959; von Oettingen, 1941; Pugh and Stone, 1968), perhaps by uncoupling oxidative phosphorylation (Kolodub and Vasilenko, 1976). The central nervous system was affected in fatal poisoning (von Oettingen, 1941). Because of the lack of subchronic and/or chronic toxicity data, as well as the inadequacy of the carcinogenicity testing, neither an ADI nor a q_1^* can be derived at this time for 2-nitrophenol, 3-nitrophenol or 4-nitrophenol.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

As indicated by the U.S. EPA (1983a,b), the lack of pertinent data regarding the chronic and/or subchronic toxicity of 2-nitrophenol, 3-nitrophenol and 4-nitrophenol precludes the derivation of RQs for these chemicals (Table 9-1).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Because of the insufficient carcinogenicity data available for 2-nitrophenol, 3-nitrophenol and 4-nitrophenol, these compounds would be classified as IARC group 3 chemicals and as group D (U.S. EPA, 1984), and, therefore, cannot be classified for their carcinogenic potential to humans.

TABLE 9-1

Nitrophenols

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:

Dose:

Effect:

Reference:

RV_d:

RV_e:

Composite Score:

RQ: Data are not sufficient for deriving an RQ.

10. REFERENCES

Alexander, H.C., K.M. Bodner and M.A. Mayes. 1983. Evaluation of the OECD "Fish Prolonged Toxicity Study at Least 14 Days". Chemosphere. 12(3): 415-423.

Alexander, M. and B.K. Lustigman. 1966. Effect of chemical structure on microbial degradation of substituted benzenes. J. Agric. Food Chem. 14(4): 410-413.

Amacher, D.E. and G.N. Turner. 1982. Mutagenic evaluation of carcinogens and noncarcinogens in the L5178Y/TK assay utilizing postmitochondrial fractions (S9) from normal rat liver. Mutat. Res. 97(1): 49-65.

Archer, T.E. 1974. Dissipation of parathion and related compounds from field-sprayed spinach. J. Agric. Food Chem. 22(6): 974-977.

Artiola-Fortuny, J. and W.H. Fuller. 1982. Adsorption of some monohydroxybenzene derivatives by soils. Soil Sci. 133: 18-22.

Atkinson, R. 1985. Kinetics and mechanisms of the gas phase reactions of the hydroxyl radical with organic compounds under atmospheric conditions. (Submitted to Chemical Reviews)

Badawy, M.I. and M.A. El-Dib. 1984. Persistence and fate of methyl parathion in sea water. Bull. Environ. Contam. Toxicol. 33(1): 40-49.

Barth, E.F. and R.L. Bunch. 1979. Biodegradation and treatability of specific pollutants. U.S. EPA, MERL, Cincinnati, OH. p. 227. EPA 600/9-79-034.

Bedient, P.B., A.C. Rodgers, T.C. Bouvette, M.B. Tomson and T.H. Wang. 1984. Groundwater quality at a creosote waste site. Ground Water. 22: 318-329.

Boutwell, R.K. and D.K. Bosch. 1959. The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res. 19: 413-424.

Boyd, S.A. 1982. Adsorption of substituted phenols by soil. Soil Sci. 134(5): 337-343.

Bracha, M. 1979. Mutagenicity of p-nitrophenol-p¹-quanidinobenzoate on Salmonella typhimurium strain TA98. Mutat. Res. 67: 81-83. (Cited in SRC, 1981)

Bringmann, G. 1975. Determination of the biologically harmful effect of water pollutants by means of the retardation of cell proliferation of the blue algae Microcystis. J. Gesund.-Ing. 96(9): 238-241.

Bringmann, G. and R. Kuhn. 1977. Befunde der Schadwirkung wassergefahrdender stoffe gegen Daphnia magna. Z.F. Waser Abwasser Forschung. 5: 161-166. (Ger.)

Bringmann, G. and R. Kuhn. 1978. Testing of substances for their toxicity threshold: Model organisms Microciptis (Diplocytis) aeruginosa and Scenedesmus quadricauda. Mitt. Inter. Verein. Limnol. 21: 274-284.

Buccafusco, R.J., S.J. Ells and G.A. LeBlanc. 1981. Acute toxicity of priority pollutants to bluegill (Lepomis machrochirus). Allied Chem. Corp., Morristown, NJ. 07960, USA. Bull. Environ. Contam. Toxicol. 26(4): 446-452.

Buselmaier, W., G. Rohrborn and P. von Propping. 1972. Mutagenitatsuntersuchungen mit pestizides im host-mediated assay und mit dem Dominanten Letaltest an der maus. Biol. Zbl. 91: 311-325. (Cited in Fahrig, 1974)

Buselmaier, W.G., G. Rohrborn and P. von Propping. 1973. Comparative investigations on the mutagenicity of pesticides in mammalian test systems. Mutat. Res. 21: 25-26.

Call, D.J., L.T. Brooke and P.Y. Lu. 1980. Uptake, elimination and metabolism of three phenols by fathead minnows. Arch. Environ. Contam. Toxicol. 9: 699-714.

Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. 1979. Water-Related Environmental Fate of 129 Priority Pollutants. Vol. II. U.S. EPA, Washington, DC. EPA-440/4-79-029B.

Cameron, M.A.M. 1958. The action of nitrophenols on the metabolic rate of rats. Western Infirmary, Glasgow, Scot. Br. J. Pharmacol. 13: 25-29.

Chambers, C.W., H.H. Tabak and P.W. Kabler. 1963. Degradation of aromatic compounds by phenol-adapted bacteria. Robt. A. Taft Sanit. Eng. Center, Cincinnati, OH. J. Water Pollut. Control Fed. 35: 1517-1528.

Chhabra, R.S. and J.R. Fouts. 1974. Sex differences in the metabolism of xenobiotics by extrahepatic tissue in rats. J. Drug Metab. Dispos. 2(4): 375-379.

Chiu, C.W., L.H. Lee, C.Y. Wang and G.T. Bryan. 1978. Mutagenicity of some commercially available nitro compounds for Salmonella typhimurium. Mutat. Res. 58(1): 11-22.

CMR (Chemical Marketing Reporter). 1984. Chemical profile - p-nitrophenol. Chem. Marketing Reporter, August 6, 1984.

Cole, R.H., R.E. Frederick, R.P. Healy and R.G. Rolan. 1984. Preliminary findings of the priority pollutant monitoring project of the Nationwide Urban Runoff Program. J. Water Pollut. Control Fed. 56(7): 898-908.

Cupitt, L.T. 1980. Fate of toxic and hazardous materials in the air environment. U.S. EPA, ESRL, Research Triangle Park, NC. EPA-600/S3-80-084.

Daughton, C.G. and D.P.H. Hsieh. 1977. Parathion utilization by bacterial symbionts in a chemostat. Appl. Environ. Microbiol. 34: 175-184.

Dedonder, A. and C.F. Van Sumere. 1971. The effects of phenolics and related compounds on the growth and respiration of Chlorella vulgaris. Z. Pflanzen. Physiol. 65: 70. (Cited in U.S. EPA, 1980)

DeWalle, F.B., D.A. Kalman, R. Dills, et al. 1982. Presence of phenolic compounds in sewage, effluent and sludge from municipal sewage treatment plants. Water Pollut. Control (Maidstone, Engl.). 14(4-5): 143-150.

Dietrich, W.C. and R. Beutner. 1946. Failure of o- or p-mono-nitrophenol to produce cataracts. Fed. Proc. 5: 174. (Cited in U.S. EPA, 1980)

Dojlido, J.R. 1979. Investigations of biodegradability and toxicity of organic compounds. Final report 1975-79. U.S. EPA, MERL, Cincinnati, OH. 118 p. EPA 600/2-79-163.

Doxtader, K.G. and M. Alexander. 1966. Nitrification by heterothrophic soil microorganisms. Soil. Sci. Soc. Am. Proc. 30: 351-355.

Ellis, D.D., C.M. Jones, R.A. Larson and D.J. Schaeffer. 1982. Organic constituents of mutagenic secondary effluents from wastewater treatment plants. Arch. Environ. Contam. Toxicol. 11(3): 373-382.

Elmamlouk, T.H. and T. Gessner. 1978. Carbohydrate and sulfate conjugations of p-nitrophenol by hepatopancreas of Homarus americanus. J. Comp. Biochem. Physiol. C. 61C(2): 363-367.

Fahrig, R. 1974. Comparative mutagenicity studies with pesticides. IARC Sci. Publ. 10: 161-181.

Fairchild. 1977. (Cited in U.S. EPA, 1980a)

Farris, R.E. 1978. Aminophenols. In: Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed., M. Grayson and D. Eckroth, Ed. John Wiley and Sons, Inc., NY. 2: 423.

Faust, S.D. 1975. Nonbiological degradation and transformations of organic pesticides in aqueous systems. ACS Sym. Ser. 18: 572-595.

Figge, K.J., J. Klohn and J. Koch. 1983. Testing of chemicals by evaluation of their distribution and degradation patterns in an environmental standard system. Reg. Toxicol. Pharmacol. 3: 199-215.

Freitag, D., H. Geyer, A. Kraus, et al. 1982. Ecotoxicological profile analysis. VII. Screening chemicals for their environmental behavior by comparative evaluation. Ecotoxicol. Environ. Saf. 6: 60-81.

Gabor, M., I. Pukovich and I. Lacson. 1962. Experimental thrombocytosis with o-nitrophenol. Naturwissenschoften. 49: 470-471. (Cited in U.S. EPA, 1980; SRC, 1981)

Garrett, N.E. and J. Lewtas. 1983. Cellular toxicity in Chinese hamster ovary cells. I. Analysis of cytotoxicity endpoints for twenty-nine priority pollutants. Environ. Res. 32(2): 455-465.

Gerike, P. and W.K. Fischer. 1979. A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox. Environ. Safety. 3: 159-173.

Gerike, P., W. Holtmann and W. Jasiak. 1984. A test for detecting recalcitrant metabolites. Chemosphere. 13: 121-141.

Gessner, T. and N. Hamada. 1974. High biliary and systematic excretion of a glucuronide during its hepatic synthesis. Life Sci. 15(1): 83-94.

Geyer, H., R. Viswanathan, D. Frieta and F. Korte. 1981. Relationship between water solubility of organic chemicals and their bioaccumulation by the alga Chlorella. Chemosphere. 10(11-12): 1307-1313.

Geyer, H., G. Politzki and D. Freitag. 1984. Prediction of ecotoxicological behavior or chemicals: Relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by alga Chlorella. Chemosphere. 13(2): 269-284.

Gilbert, P.A. and C.M. Lee. 1980. Biodegradation tests: Use and value. In: Biotransformation and Fate of Chemicals in the Aquatic Environment, A.W. Maki, K.L. Dickson and J.Cairns, Jr., Ed. Proc. of a Workshop held at Univ. of Mich. Biol. St.

Gram, T.E., C.L. Litterst and E.G. Mimnaugh. 1974. Enzymic conjugation of foreign chemical compounds by rabbit lung and liver. J. Drug Metab. Dispos. Biol. Fate Chem. 2(3): 254-258.

Grant, C.M. 1959. The action of nitrophenols on the pulmonary ventilation of rats. Br. J. Pharmacol. 14: 401-403.

Grosch, D.S. 1973. Reproduction tests. The toxicity for Artemia of derivatives from nonpersistent pesticides. J. Biol. Bull. 145(2): 340-351.

Gunther, K., W.G. Filby and K. Eiben. 1971. Hydroxylation of substitute phenols: An ESR-study in the Ti^{3}/H_2O_2 system. Tetrahedron Lett. 3: 251-254. (Cited in Callahan et al., 1979)

Gvozdyak, P.I, A.V. Livke, V. Udod, S.P. Bykova, G.N. Dmitrenko and L.V. Reznik. 1982. Transformation of p-nitrophenol by Bacillus and Pseudomonas bacteria. Mikrobiol. Zh. (Kiev). 44(1): 12-15. (CA 97:52251e)

Halbach, U., M. Siebert, M. Westermayer and C. Wissel. 1983. Poplulation ecology of rotifers as a bioassay tool for ecotoxicological tests in aquatic environments. Ecotoxicol. Environ. Saf. 7(5): 484-513.

Haller, H.D. 1978. Degradation of mono-substituted benzoates and phenols by wastewater. J. Water Pollut. Control Fed. 50(12): 2771-2777.

Hansch, C. and A.J. Leo. 1981. Medchem Project. Issue No. 19, Pomona College, Claremont, CA.

Hawley, G.C. 1977. The Condensed Chemical Dictionary, 9th ed. Van Nostrand Reinhold Co., NY. p. 618.

Haworth, S., T. Lawlor, K. Mortelmans, W. Speck and E. Zeiger. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ. Mutat. Suppl. 1: 3-142.

Heitmuller, P.T., T.A. Hollister and P.R. Parpish. 1981. Acute toxicity of 54 industrial chemicals to sheepshead minnows (Cyprinodon variegatus). Bull. Environ. Contam. Toxicol. 27(5): 596-604.

Ho, Y.L. and S.K. Ho. 1981. Screening of carcinogens with the prophase c2Its857 induction test. Cancer Res. 41(2): 532-536.

Hodson, P.V., D.G. Dixon and K.L.E. Kaiser. 1984. Measurement of median lethal dose as a rapid indication of contaminant toxicity to fish. Environ. Toxicol. Chem. 3(2): 245-254.

Holcombe, G.W., G.L. Phipps, L. Gary, M.L. Knuth and T. Felhaber. 1984. The acute toxicity of selected substituted phenols, benzenes and benzoic acid esters to fathead minnows (Pimephales promelas). Environ. Pollut., Ser. A. 35(4): 367-381.

Howard, P.H., J. Santodonato, J. Saxena, J. Malling and D. Greninger. 1976. Investigation of selected potential environmental contaminants: Nitroaromatics (Draft). U.S. EPA, Research Triangle Park, NC. 600 p. EPA 560/2-76-010.

Huang, J. and E. Gloyna. 1967. Effects of toxic organics on photosynthetic reoxygenation. Environ. Health Eng. Res. Lab. p. 216-749. (Cited in U.S. EPA, 1980)

Hustert, K., M. Mansour, H. Parlar and F. Korte. 1981. The EPA test - A method to determine the photochemical degradation of organic compounds in aquatic systems. Chemosphere. 10: 995-998.

Joergensen, L. and T. Johansen. 1983. Affinity of drugs for cytochrome P-450 determined by inhibition of p-nitrophenetole O-deethylation by rat liver microsomes. Acta Pharmacol. Toxicol. 53(1): 70-77.

Johnson, L.D. and J.C. Young. 1983. Inhibition of anaerobic digestion by organic priority pollutants. J. Water Pollut. Control Fed. 55: 1441-1449.

Kawasaki, M. 1980. Experience with the test scheme under the chemical control law of Japan: An approach to structure-activity correlations. Ecotoxicol. Environ. Saf. 4: 444-454.

Kenaga, E.E. and C.A.I. Goring. 1978. Relationship between water solubility, soil-sorption, octanol-water partitioning, and bioconcentration of chemicals in biota. Prepublication copy of paper dated Oct. 13, 1978, given at the Third Aquatic Toxicology Symposium, American Society for Testing and Materials, New Orleans, LA, October 17-18, 1978.

Kitano, M. 1978. Biodegradation and Bioaccumulation Test on Chemical Substances. OECD Tkyo Meeting, Ref. Book TSU-No.3.

Klein, W., H. Geyer, D. Freitag and H. Rohleder. 1984. Sensitivity of schemes for ecotoxicological hazard ranking of chemicals. Chemosphere. 13(1): 203-211.

Kolodub, F.A. and N.M. Vasilenko. 1976. Characteristics of disturbances in oxidation and phosphorylation processes in rat liver caused by mono-nitrophenols. Ukr. Bikhim. Zh. 48(2): 30-33. (CA 84:100380b)

Kool, H.J. 1984. Influence of microbial biomass on the biodegradability of organic compounds. Chemosphere. 13(7): 751-761.

Kopperman, H.L., R.M. Carlson and R. Caple. 1974. Aqueous chlorination and ozonation studies. I. Structure-toxicity correlations of phenolic compounds to Daphnia magna. Chem. Biol. Interact. 9(4): 245-251.

Kotzias, D., H. Parlar and F. Korte. 1982. Photoreactivity of organic chemicals in water in the presence of nitrate and nitrite. Naturwissenschaften. 69: 444-445.

Kramer, N. and R.N. Doetsch. 1950. The growth of phenol-utilizing bacteria on aromatic carbon sources. Arch. Biochem. Biophys. 26: 401-405.

Laitinen, M., M. Nieminen and E. Hietanen. 1982. The effect of pH changes of water on the hepatic metabolism of xenobiotics in fish. Acta Pharmacol. Toxicol. 51(1): 24-29.

Lammering, M.W. and N.C. Burbank. 1960. The toxicity of phenol, p-chlorphenol and o-nitrophenol to bluegill sunfish. Eng. Bull. Purdue Univ. Eng. Ext. Serv. 106: 541-555. (CA 55:27671c) (Cited in U.S. EPA, 1980)

Landrum, P.F. and D.G. Crosby. 1981. Comparison of the disposition of several nitrogen-containing compounds in the sea urchin and other marine invertebrates. J. Xenobiotica. 11(5): 351-361.

Lawford, D.J., E. King and D.G. Harvey. 1954. On the metabolism of some aromatic nitrocompounds by different species of animals. J. Pharm. Pharmacol. 6: 619-624. (Cited in SRC, 1981)

LeBlanc, G.A. 1980. Acute toxicity of priority pollutants to water flea (Daphnia magna). Bull. Environ. Contam. Toxicol. 24(5): 684-691.

LeBlanc, G.A. 1984. Interspecies relationships in acute toxicity of chemicals to aquatic organisms. Environ. Toxicol. Chem. 3(1): 47-60.

Lemaire, J., I. Campbell, H. Hulpke, et al. 1982. An assessment of test methods for photodegradation of chemicals in the environment. Chemosphere. 11: 119-164.

Litterst, C.L., and E.P. Lichtenstein. 1971. Effects and interactions of environmental chemicals on human cells in tissue culture. Arch. Environ. Health. 22(4): 454-459.

Liu, D. 1981. Biodegradation of p-nitrophenol in aqueous medium. Div. Contam. Environ., Inst. Natl. Rech. Eaus, Burlington, ON, Can., L7R 4A6. J. Eau Que. 14(3): 212-213.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Co., NY. p. 15-16.

Mabey, W.R., J.H. Smith, R.T. Podoll, et al. 1981. Aquatic Fate Process Data for Organic Priority Pollutants. Monitoring and Data Support Division, Office of Water Regulations and Standards, Washington, DC. EPA 440/4-81-014.

Machida, M., Y. Morita, M. Hayashi and S. Awazu. 1982. Pharmacokinetic evidence for the occurrence of extrahepatic conjugative metabolism of p-nitrophenol in rats. Biochem. Pharmacol. 31(5): 787-791.

Makhinya, A.P. 1969. Comparative hygienic and sanitary-toxicological studies of nitrophenol isomers in relation to their normalization in reservoir waters. Prom. Zasryazneniya Vodoemov. 9: 84-95.

Matsuguma, H.J. 1967. Nitrophenols. In: Kirk-Othmer Encyclopedia of Chemical Technology, 2nd ed., A. Standen, Ed. John Wiley and Sons, Inc., NY. Vol. 13, p. 888-894.

McCann, J., E. Choi, E. Yamasaki and B.N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. Proc. Natl. Acad. Sci. 72: 5135-5139.

McCormick, N.G., F.E. Feeherry and H.S. Levinson. 1976. Microbial transformation of 2,4,6-trinitrotoluene and other nitroaromatic compounds. Appl. Environ. Microbiol. 32(6): 949-958.

McLeese, D.W., V. Zitko and M.R. Peterson. 1979. Structure-lethality relationships for phenols, anilines and other aromatic compounds in shrimp and clams. Chemosphere. 8(2): 53-57.

Means, J.L. and S.J. Anderson. 1981. Comparison of five different methods for measuring biodegradability in aqueous environments. Water, Air, Soil Pollut. 16(3): 301-315.

Mitra, D. and C.S. Vaidyanathan. 1982. Comparative phytotoxicity soil pollutants and their microbial metabolites to the growth of cucumber (Cucumis sativus L.) seedlings. Plant Soil. 69(3): 467-471.

Moldeus, P. H. Vadi and M. Berggren. 1976. Oxidative and conjugative metabolism of p-nitrophenol in isolated rat liver cells. Acta Pharmacol. Toxicol. 39(1): 17-32.

Motais, R., F. Sola and J.L. Cousin. 1978. Uncouplers of oxidative phosphorylation. A structure-activity study of their inhibitory effect on passive chloride permeability. Biochem. Biophys. Acta. 510(1): 201-207.

Muller, W.U., C. Streffer and N. Zamboglou. 1981. Effects of a combine. treatment with x-rays and phenols on preimplantation mouse embryos in vitr. J. Radiat. Environ. Biophys. 19(4): 247-258.

Nagel, R. and K. Urich. 1980. Kinetic studies on the elimination of different substituted phenols by goldfish (Carassius auratus). J. Bull. Environ. Contam. Toxicol. 24(3): 374-378.

Nagel, R. and K. Urich. 1981. Elimination and distribution of different substituted phenols by frog (Rana temporaria) and crayfish (Astacus leptodactylus). Bull. Environ. Contam. Toxicol. 26(3): 289-294.

Nakagawa, M. and D.G. Crosby. 1974. Photodecomposition of nitrofen. J. Agric. Food Chem. 22: 849-853.

Neujahr, H.Y. and J.M. Varga. 1970. Degradation of phenols by intact cells and cell free preparation of Trichosporon cutaneum. Eur. J. Biochem. 13: 37-44.

Neujarh, H.Y., S. Lindsjo and J.M. Varga. 1974. Oxidation of phenols by cells and cell-free enzyme from Candida tropicalis. J. Antonie van Leeuwenhoek. J. Microbiol. Serol. 40(2): 209-216.

Nojima, K., K. Fukaya, S. Kanno, S. Nishiyama and Y. Wada. 1976. Studies on photochemistry of aromatic hydrocarbons. III. Chemosphere. 1: 25-30.

Nojima, K., A. Kawaguchi, T. Ohya, S. Kanno and M. Hirobe. 1983. Studies on photochemical reaction of air pollutants. X. Identification of nitrophenols in suspended particulates. Chem. Pharm. Bull. 31(3): 1047-1051.

NTP (National Toxicology Program). 1984. Chemicals on standard protocol, carcinogenesis testing program. October 25, 1984.

Oberly, T.J., B.J. Bewsey and G.S. Probst. 1984. An evaluation of the L-5178Y TK+/- mouse lymphoma forward mutation assay using 42 chemicals. Mutat. Res. 125(2): 291-306.

Ogino, S. and K. Yasukura. 1957. Biochemical studies on cataract. VI. Production of cataracts in guinea pigs with dinitrophenol. Am. J. Ophthalmol. 43: 936-946. (Cited in U.S. EPA, 1980; SRC, 1981)

Paris, D.F., N.L. Wolfe and W.C. Steen. 1982. Structure-activity relationships in microbial transformation of phenols. J. Appl. Environ. Microbiol. 44(2): 153-158.

Paris, D.F., N.L. Wolfe, W.C. Steen and G.L. Baughman. 1983. Effect of phenol molecular structure on bacterial transformation rate constants in pond and river samples. Appl. Environ. Microbiol. 45: 1153-1155.

Perry, R.H. and C.H. Chilton. 1973. Chemical Engineers' Handbook, 5th ed. McGraw-Hill Book Co, NY. p. 3-58.

Phipps, G.L., G.W. Holcombe and J.T. Fiandt. 1981. Acute toxicity of phenol and substituted phenols to the fathead minnow. Bull. Environ. Contam. Toxicol. 26(5): 585-593.

Pitter, P. 1976. Determination of biological degradability of organic substances. Water Res. 10(3): 231-235.

Poirier, M.C., B.T. DeCicco and M.W. Lieberman. 1975. Nonspecific inhibition of DNA repair synthesis by tumor promoters in human diploid fibroblasts damaged with N-acetoxy-2-acetylaminofluorene. Cancer Res. 35(6): 1392-1397.

Probst, G.S., R.E. McMahon, L.E. Hill, C.Z. Thompson, J.K. Epp and S.B. Neal. 1981. Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures: A comparison with bacterial mutagenicity using 218 compounds. Environ. Mutagen. 3(2): 11-32.

Pugh, P.M. and S.L. Stone. 1968. The effect of 2,4-dinitrophenol and related compounds on bile secretion. J. Physiol. 198: 39-49. (Cited in SRC, 1981)

Raymond, D.G.M. and M. Alexander. 1971. Microbial metabolism and cometabolism of nitrophenols. Pestic. Biochem. Physiol. 1: 123-130.

Reinke, L.A., F.C. Kauffman, R.K. Evans, S.A. Belisky and R.G. Thurman. 1979. p-Nitrophenol conjugation in perfused livers from normal and phenobarbital-treated rats: Influence of nutritional state. Res. Commun. Chem. Pathol. Pharmacol. 23(1): 185-193.

Reinke, L.A., S.A. Belinsky, R.K. Evans, F.C. Kauffman and R.G. Thurman. 1981. Conjugation of p-nitrophenol in the perfused rat liver: The effect of substrate concentration and carbohydrate reserves. J. Pharmacol. Exp. Ther. 217(3): 863-870.

Rickert, D.E., J.A. Bond, R.M. Long and J.P. Chism. 1983. Metabolism and excretion of nitrobenzene by rats and mice. Toxicol. Appl. Pharmacol. 67(2): 206-214.

Robinson, D., J.N. Smith and R.T. Williams. 1951. Studies in detoxication. 39. Nitro compounds (a) The metabolism of o-, m-, and p-nitrophenols in the rabbit. (b) The glucuronide of the mono-nitrophenols and observations on the anomalous optical rotations of triacetyl β-o-nitrophenol glucuronide and its methyl ester. Biochem. J. 50: 221-227.

Rott, B., R. Viswanathan, D. Freitag and F. Korte. 1982. Comparison of the applicability of various tests for screening the degradability of environmental chemicals. Chemosphere. 11: 531-538.

Rubin, H.E. and M. Alexander. 1983. Effect of nutrients on the rates of mineralization of trace bioconcentrations of phenol and nitrophenol. Environ. Sci. Technol. 17: 104-107.

Rugstad, H.E. and E. Dybing. 1974. Competition between p-aminophenol, p-nitrophenol, and bilirubin for glucuronidation in cultures of rat hepatoma cells and homogenates of the same cells. J. Acta Pharmacol. Toxicol. 34(1): 65-76.

Rugstad, H.E. and E. Dybing. 1975. Glucuronidation in cultures of human skin epithelial cells. J. Eur. J. Clin. Invest. 5(2): 133-137.

Saarikoski, J. and M. Viluksela. 1982. Relation between physicochemical properties of phenols and their toxicity and accumulation in fish. Ecotoxicol. Environ. Saf. 6(6): 501-512.

Sabljic, A. 1984. Predictions of the nature and strength of soil sorption or organic pollutants by molecular topology. J. Agric. Food Chem. 32: 243-246.

Sadtler. 1960. Sadtler UV spectracard. m-Nitrophenol. Samuel P. Sadtler & Sons, Philadelphia, PA.

Saltzman, S. and S. Yariv. 1975. Infrared study of the sorption of phenol and p-nitrophenol by montmorillonite. Proc. Soil Sci. Soc. Am. 39(3): 474-479. (Cited in Callahan et al., 1979)

Sasaki, S. 1978. The scientific aspects of the chemical substance control law in Japan. In: Aquatic Pollutants: Transformation and Biological Effects, O. Hutzinger, L.H. von Letyoeld and B.C.J. Zoeteman, Ed. Pergamon Press Oxford. p. 283-298.

Scala, A.J. and S. Banerjee. 1982. Vapor pressure interlaboratory report. Prepared by Syracuse Research Corporation. Final Report for National Bureau of Standards, 8 p. and Appendices.

Schmidt-Sonnenschein, B. 1977. Metabolism of (Ohenyl-U-14C) parathion and p-nitrophenol metabolites in the rat. Ber. Kernforschunssanlase Juelich. 1450(0366-0885): 112 p. (CA 88:165115W)

Schultz, B. 1983. Determination of priority pollutant nitrophenols in water by high-performance liquid chromatography. J. Chromatogr. 269(3): 208-212.

Serjeant, E.P. and B. Dempsey. 1979. Ionisation constants of organic acids in aqueous solution. IUPAC Chemical Data Series. Pergamon Press, NY. 989 p.

Shackelford, W.M. and L.H. Keith. 1976. Frequency of organic compounds identified in water. U.S. EPA, Athens, GA. EPA-600/4-76-062.

Shelton, D.R. and J.M. Tiedje. 1984. General method for determining anaerobic biodegradation potential. Appl. Environ. Microbiol. 47(4): 850-857.

Shen, T.C.R. 1962. The stimulating effect of dinitro-ortho-cresol, dinitrophenol and paranitrophenol on the aortic chemoreceptors in dogs. Arch. Int. Pharmacodyn. CXL (3-4): 521-527. (Cited in SRC, 1981)

Smith, R.P., A.A. Alkaitis and P.R. Shafer. 1967. Chemically induced methemoglobinemia in the mouse. Biochem. Pharmacol. 16: 317-328. (Cited in U.S. EPA, 1980)

Smith, G.S., J.B. Watkins, T.N. Thompson, K. Rozman and C.D. Klaassen. 1984. Oxidative and conjugative metabolism of xenobiotics by livers of cattle, sheep, swine and rats. J. Anim. Sci. 58(2): 386-395.

Snodgrass, H.L., Jr. 1983. Dermal penetration and distribution of carbon-14-labeled para-nitrophenol (PNP) February-April 1983. Phase 1. Report, USAEHA-75-51-0047-84; Order No. Ad-A134315, 15 p. Avail. NTIS from: Gov. Rep. Announce. Index (U.S.) 1984, 84(4): 70.

Sonawane, B.R., P.M. Coates, J. Sumner and O. Koldovsky. 1983. Influence of dietary carbohydrates (α-saccharides) on hepatic drug metabolism in male rats. Drug-Nutr. Interact. 2(1): 7-16. (CA 98:214543b)

Sorimachi, M. and K. Yamagami. 1982. Nitrophenol compounds induce calcium-dependent exocytotic secretion of catecholamines by a direct effect on the plasma membranes of the adrenal medullary cells. Brain Res. 232(1): 242-246.

Spain, J.C. and P.A. Van Veld. 1983. Adaptation of natural microbial communities to degradation of xenobiotic compounds: Effects of concentration, exposure time, inoculum, and chemical structure. Appl. Environ. Microbiol. 45(2): 428-435.

Spain, J.C., O. Wyss and D.T. Gibson. 1979. Enzymic oxidation of p-nitrophenol. Biochem. Biophys. Res. Commun. 88(2): 634-641.

Spain, J.C., P.H. Pritchard and A.W. Bourquin. 1980. Effects of adaptation on biodegradation rates in sediment/water cores from estuarine and freshwater environments. Appl. Environ. Microbiol. 40(4): 726-734.

SRC (Syracuse Research Corporation). 1981. Information profiles on potential occupational hazards: Nitrophenols. Prepared under Contract 210-79-0030 for the National Institute for Occupational Safety and Health, 5600 Fishers Lane, Rockville, MD 20857.

SRI (Stanford Research Institute). 1984. 1984 Directory of Chemical Producers: United States of America. SRI International, Menlo Park, CA.

Stofen, D. 1973. The maximum permissible concentration in the U.S.S.R. for harmful substances in drinking water. Toxicology. 1: 187-195. (Cited in U.S. EPA, 1980)

Suarez, C., F. Louys, K. Gunther and K. Eiben. 1970. Hydroxyl radical induced denitration of nitrophenols. Tetrahedron Lett. 8: 575-578. (Cited in Callahan et al., 1979)

Subba-Rao, R.V., H.E. Rubin and M. Alexander. 1982. Kinetics and extent of mineralization of organic chemicals at trace levels in freshwater and sewage. Appl. Environ. Microbiol. 43: 1139-1150.

Sudhakar-Barik and N. Sethunathan. 1978. Metabolism of nitrophenols in flooded soils. J. Environ. Qual. 7(3): 349-352.

Sudhakar-Barik, R. Siddaramappa and N. Sethunathan. 1976. Metabolism of nitrophenols by bacteria isolated from parathion-amended flooded soil. Antonie van Leeuwenhoek. 42(4): 461-470.

Sudhakar-Barik, R. Siddaramappa, P.A. Wahid and N. Sethunathan. 1978. Conversion of p-nitrophenol to 4-nitrocatechol by a Pseudomonas sp. Antonie van Leeuwenhoek. 44(2): 171-176.

Sudhakar-Barik, P.A. Wahid, C. Ramakrishna and N. Sethunathan. 1979. A change in the degradation pathway of parathion after repeated applications to flooded soil. J. Agric. Food Chem. 27: 1391-1392.

Sultatos, L.G. and S.D. Murphy. 1983. Hepatic microsomal detoxification of the organophosphates paraoxon and chlorphyrifos oxon in the mouse. Drug Metab. Dispos. 11(3): 232-238.

Suzuki, J. T. Koyama and S. Suzuki. 1983. Mutagenicities of mononitrobenzene derivatives in the presence of norharman. Mutat. Res. 120(2-3): 105-110.

Szybalski, W. 1958. Special microbiological systems. Observations on chemical mutagenesis in microorganisms. Ann. NY Acad. Sci. 76: 475-489.

Tabak, H.H., C.W. Chambers and P.W. Kabler. 1964. Microbial metabolism of aromatic compounds. I. Decomposition of phenolic compounds and aromatic hydrocarbons by phenol-adapted bacteria. J. Bacteriol. 87: 910-919.

Tabak, H.H., S.A. Quave, C.I. Mashni and E.F. Barth. 1981. Biodegradability studies with organic priority pollutant compounds. J. Water Pollut. Control Fed. 53(10): 1503-1518.

Taylor, G. 1979a. Chief, Laboratory Investigations Branch, DRDS, NIOSH. Written communication dated June 12, 1979, to Mutagenicity Task Force, NIOSH, regarding mutagenicity testing of ortho- and para-nitrophenols. (Cited in SRC, 1981)

Taylor, G. 1979b. Chief, Laboratory Investigations Branch, DRDS, NIOSH. Written communication dated June 12, 1979, to Mutagenicity Task Force, NIOSH, regarding mutagenicity testing of meta-nitrophenol. (Cited in SRC, 1981)

Tewfik, M.S. and Y.A. Hamdi. 1975. Metabolism of fluorodifen by soil microorganisms. Soil Biol. Biochem. 7(2): 79-82.

Thurman, R.G., L.A. Reinke, S. Belinsky, R.K. Evans and F.C. Kauffman. 1981. Coregulation of the mixed-function oxidation of p-nitroanisole and glucuronidation of p-nitrophenol in the perfused rat liver by carbohydrate reserves. Arch. Biochem. Biophys. 209(1): 137-142.

Tonda, K. and M. Hirata. 1983. Glucuronidation and sulfation of p-nitrophenol in isolated rat hepatocyte subpopulations. Effect of phenobarbital and 3-methylcholanthrene pretreatment. Chem. Biol. Interact. 47(3): 277-287.

Tonogai, Y., S. Yasuhide, I. Shunjiro, Y. Ito and M. Iwaida. 1982. Actual survey on TLm (median tolerance limit) values of environmental pollutants, especially on amines, nitriles, aromatic nitrogen compounds and artificial dyes. J. Toxicol. Sci. 7(3): 193-203.

Tremaine, L.M., G.L. Diamond and A.J. Quebbemann. 1984. In vivo quantification of renal glucuronide and sulfate conjugation of 1-naphthol and p-nitrophenol in the rat. Biochem. Pharmacol. 33(3): 419-427.

U.S. EPA. 1977. Computer printout of non-confidential production data from TSCA Inventory. U.S. EPA, OPTS, CID, Washington, DC.

U.S. EPA. 1978. In-depth Studies on Health and Environmental Impacts of Selected Water Pollutants. Prepared by E.G. and G. Bionomics, Wareham, MA. Contract No. 68-01-4646 for U.S. EPA, Washington, DC.

U.S. EPA. 1980a. Ambient Water Quality Criteria for Nitrophenols. U.S. EPA, ECAO, Cincinnati, OH. NTIS PB 81-117749.

U.S. EPA. 1980b. Carbon Adsorption Isotherms for Toxic Organics. Municipal Environmental Research Labs., Cincinnati, OH. EPA-600/8-80-023.

U.S. EPA. 1983a. Reportable Quantity Document for p-Nitrophenol. External review draft. Prepared by U.S. EPA, ECAO, Cincinnati, OH. ECAO-CIN-R170.

U.S. EPA. 1983b. Reportable Quantity Document for 2-Nitrophenol. External review draft. Prepared by U.S. EPA, ECAO, Cincinnati, OH. ECAO-CIN-R171.

U.S. EPA. 1984. Guidelines for Cancer Risk Assessment. Federal Register. 49(227): 46294-46301.

USITC (U.S. International Trade Commission). 1984a. Synthetic Organic Chemicals. U.S. Production and Sales, 1983. USITC Publ. 1588. U.S. International Trade Commission, Washington, DC.

USITC (U.S. International Trade Commission). 1984b. Imports of Benzenoid Chemicals and Products. 1983. USITC Publ. 1548. p. 24. U.S. International Trade Commission, Washington, DC.

Van Veld, P.A., J.C. Spain. 1983. Degradation of selected xenobiotic compounds in three types of aquatic test systems. Chemosphere. 12(9-10): 1291-1305.

Vasilenko, N.M., V.A. Volodchenko, T. S. Baturina and F.A. Kolodub. 1976. Toxicological characteristics of mono-nitrophenols with regard to their isomeric form. Farmakol. Tosikol. (Moscow). 39(6): 718-721. (CA 86:12433g)

Veith, G.D., D.L. Delore and B.V. Bergstedt. 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. J. Fish Res. Board Can. 36: 1040-1048.

Veith, G.D., K.J. Macek, S.R. Petrocelli and J. Carroll. 1980. An evaluation of using partition coefficients and water solubility to estimate bioconcentration factors for organic chemicals in fish. In: Aquatic Toxicology, ASTM STP707, J.G. Eaton, P.R. Parrish and A.C. Hendricks, Ed. American Society for Testing and Materials. p. 116-129.

Vernot, E.H., J.D. MacEwen, C.C. Haun and E.R. Kinkead. 1977. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. Toxicol. Appl. Pharmacol. 42(2): 417-423.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY. p. 917-920.

von Oettingen, W.F. 1941. The aromatic amino and nitro compounds, their toxicity and potential dangers. A review of the literature. U.S. Pub. Health Bull. 271: 130-155. (Cited in U.S. EPA, 1980; SRC, 1981)

von Propping, P., W. Buselmaier and G. Rohrborn. 1973. Kritische betrachtung uber die intra--animale kultire von microorganismen, eine methode zum Nachweiss chemisch induzierter mutationen. Arzneim-Forsch. 23: 746-749. (Ger.)

Ward, G.S., P.R. Parrish and R.A. Risby. 1981. Early life stage toxicity tests with a saltwater fish: Effects of eight chemicals on survival, growth, and development of sheepshead minnows (Cyprinodon variegatus). J. Toxicol. Environ. Health. 8(1-2): 225-240.

Weast, R.C. 1972. Handbook of Chemistry and Physics, 53rd ed. The Chemical Rubber Co., Cleveland, OH.

Weber, R.C., P.A. Parker and M. Bowser. 1981. Vapor pressure distribution of selected organic chemicals. U.S. EPA, Cincinnati, OH. 39 p. EPA 600/2-81-021.

Wilson, J.T. and B.H. Smith. 1981. Biodegradation of phenol 2 chlorinated phenols and nitrophenol in soil. SISI Annual Meeting of the American Society for Microbiology, Dallas, TX, USA, March 1-6, 1981. Abstr. Ann. Meeting Am. Soc. Microbiol. 81(0). p. 206.

Wishart, G.J. and G.J. Dutton. 1977. Precocious development *in utero* of certain UDP-glucuronyltransferase activities in rat fetuses exposed to glucocorticoids. Biochem. Biophys. Res. Commun. 75(1): 125-129.

Yeary, R.A. and M. Fleming. 1971. Developmental changes in p-nitrophenol glucuronidation in the Gunn rat. Biochem. Pharmacol. 20(2): 375-378.

Yoshimura, H., S. Ida, H. Tsuji, M. Mori and H. Ysukamoto. 1967. Metabolism of drugs. LVII. Isolation, characterization, and identification of p-nitrophenoxyacetic acid, a metabolite of butyl p-nitrophenyl ether in rats, mice, and guinea pigs. Biochem. Pharmacol. 16(10): 1953-1958.

Young, D.R., R.W. Gossett, R.B. Baird, D.A. Brown, P.A. Taylor and M.J. Miille. 1983. Wastewater inputs and marine bioaccumulation of priority pollutant organics off southern California. Water Chlorination: Environ. Impact Health Eff. 4(2): 871-884.

Zahn, R. and H. Wellens. 1980. Examination of biological degradability through the batch method - Further experience and new possibilities of usage. Z. Wasser Abwasser Forsch. 13: 1-7.

Zeyer, J. and P.C. Kearney. 1984. Degradation of o-nitrophenol and m-nitrophenol by a *Pseudomonas putida*. J. Agric. Food Chem. 32(3): 238-242.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in December, 1984. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

ACGIH (American Conference of Governmental Industrial Hygienists). 1983. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1983-1984. Cincinnati, OH. 94 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technology Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

NTP (National Toxicology Program). 1984. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1984. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1982. Chemical Activities Status Report, 3rd ed. (EPACASR). Offices of Pesticides and Toxic Substances, Washington, DC. EPA 560/TIIS-82-002b.

U.S. EPA. 1983. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1984. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422. Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under contract No. 68-01-0007, Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Service. Resource Publ. 137. Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California. State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.